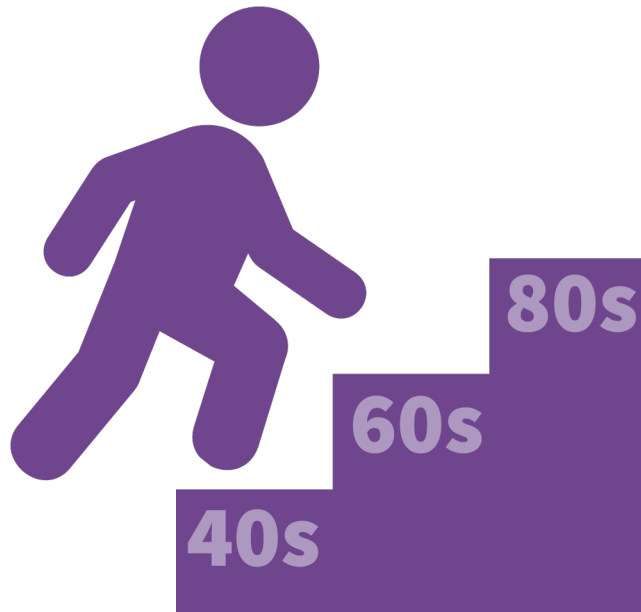


Examine[®]

Healthy Aging Supplement Guide



Written By: Michael Hull, & Wyatt Brown

Edited By: Pierre-Alexandre Sicart

Reviewed By: Kamal Patel

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Introduction

Ever notice how differently people seem to age, appearance-wise? For every 35-year-old who looks 50, there is a 50-year-old trending toward mid 30s in appearance.

Although we all experience time in the same way, the months, days, and years seem to be more kind to some than others. The good news is that we can partially control the effects of time on our bodies. And this is precisely why we wrote this guide. We can't stop the forward march of time, but we do have a say in the resilience of our minds and bodies.

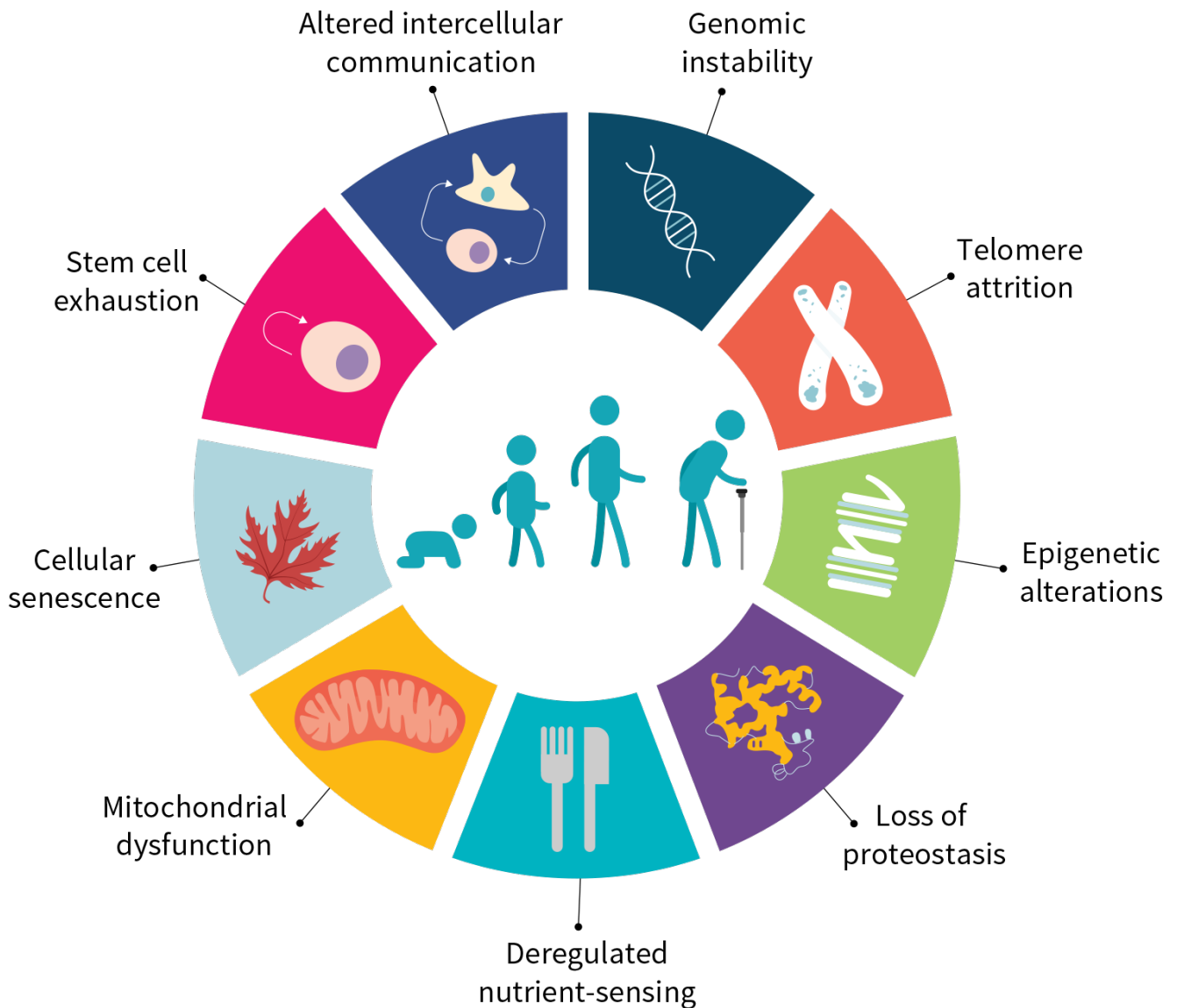
A definition for aging

Before we discuss healthy aging, it helps to start with a good understanding of what aging is. According to a recent review, aging can be *“characterized by a progressive loss of physiological integrity, leading to impaired function and increased vulnerability to death.”*^[1]

Well, that's encouraging!

Although this sounds dismal — scientists are not ones to sugarcoat — there are actually some things here to be encouraged by. We understand the aging process and mechanisms behind it now more than ever. With this knowledge, we're better positioned to exert some control over it.

The hallmarks of aging



Adapted from López-Otín et al. *Cell*. 2013.^[1]

Lifespan vs. healthspan

The average human lifespan has increased quite a bit in the past 100 years, but the extra time spent on this earth isn't always in good health. The longer humans live, the more prevalent late-onset diseases, such as diabetes, [Parkinson's](#), and [Alzheimer's](#), become. Adding 40 years of life isn't so great if the latter 40 are spent battling a devastating disease. This brings up an important concept: lifespan vs. healthspan. While lifespan, as you might expect, is the *length* of one's life, healthspan is more concerned with *quality of life*, or the time period during life where you are in a healthy and high-functioning state. For example, the current average lifespan in the U.S. is around 79 years,^[2] while the average [healthspan is only 67.4](#).

Science has made good progress in the past 25 years, increasing our understanding of the genetic and biological factors that control lifespan. But much of this may be hardwired across different organisms and less accessible with current technology.^[3] Healthspan, on the other hand, is very much within our reach and the focus of this guide.

 **Tip: Choose your own learning adventure**

If you want to learn about the process of aging, check out the [biological aspects of aging](#) section. If you want to learn about practical steps to take to age well, check out the [strategies for healthy aging](#) section.

The biological aspects of aging

Genomic instability and senescence

Taking a “macro” perspective on aging, the effects of large swaths of time on the human body are easy to recognize. There are effects on appearance (wrinkles, gray hair, loss of muscle mass, poor posture) as well as physical health (cognitive decline, increased incidence of chronic and degenerative disease). These noticeable, *macroscopic* changes on the downward side of healthspan are driven by *microscopic* changes at the cellular and molecular level.

Most scientists in the cancer biology field have come to the consensus that if we live long enough, we will get cancer. The reason for this is that the genome becomes unstable over time, leading to an accumulation of mutations that eventually transform normal, well-behaved cells into cancerous ones. Packed tightly into the nucleus of every cell and organized into chromosomes, the blueprint for every protein, enzyme, cell, and tissue is encoded by a double-stranded miracle molecule known as DNA. Because cells have a limited lifespan, this information needs to be copied and passed on to daughter cells with a high degree of fidelity.

To illustrate how daunting a task this is, human chromosomes [range in size](#) from 50 million to over 300 million nucleotides. No enzyme that copies DNA is perfect; although infrequent, there is a high probability that at least some mistakes will be made with each cell division. This is why huge amounts of resources are committed to DNA repair and quality control.^[4]

If the error can't be repaired, there are still options. Some cells will sacrifice themselves, undergoing a form of programmed cell death called apoptosis. In other cases, the cell will enter a state of “senescence,” or permanent exit from the cell cycle. By shutting down the cell cycle, senescent cells avoid copying compromised DNA that could lead to cell transformation and cancer. It is a common feature of aging in a number of different organisms, from bacteria to humans.^[5]

While senescent cells do not have the ability to divide and pass on their potentially dangerous mutated DNA, there are still downsides to consider. Senescent cells tend to secrete pro-inflammatory cytokines, contributing to the low-level chronic inflammation that appears with increasing age. This inflammation is so common that it's even been given a catchy name: “inflamm-aging”.^[6]

Stem cell exhaustion

The amazing thing about the human body is that much of our tissue has the ability to regenerate and stay

functional, through the use of stem cells. Skeletal muscle is a great example of this specialized cell in action. Let's say you do a heavy weight-training workout, which causes damage to the muscle in the form of microtrauma. In addition to rebuilding and repairing damage in the existing muscle cells, satellite cells — a specialized pool of muscle stem cells — are called on during the growth and adaptation process^[7] to fuse with existing muscle fibers, contributing more nuclei.^[8] In the case of more severe muscle damage, from injury, satellite cells differentiate into myoblasts, which continue to divide and eventually transform into myocytes (mature muscle cells) that replenish the damaged or destroyed cells.^[9]

Once called on, the satellite cells “self-renew,” ensuring that a pool of stem cells remains at the ready for the next injury or microtrauma. Other pools of stem cells are present all over the body, where they drive tissue regeneration and have the ability to self-renew. As you might expect, stem cells cannot self-renew forever. Eventually, with increasing age, they become exhausted,^[10] in part due to the accumulation of DNA damage.

Mitochondrial dysfunction

Mitochondria are the tiny power plants inside cells that generate the main energy currency in the body, *adenosine triphosphate* (ATP). They do this through cellular respiration, a process that uses the chemical energy from glucose or other nutrients to make ATP. During this process, electrons are shuttled through the electron transport chain, a series of molecules in the outer mitochondrial membrane that fuel the activity of a membrane-bound enzyme that produces ATP. As we age, the electron transport chains can become dysfunctional and “leaky,” releasing toxic *reactive oxygen species* (ROS) and producing less ATP.^[11] At one time, scientists believed that increased ROS from mitochondria was the root cause of all aging.^[12] We now know it's more complicated, since ROS has also been found to function as an important signaling molecule, and mice engineered to have impaired mitochondrial function without increased ROS still had accelerated aging.^[13] Nonetheless, the accumulation of dysfunctional mitochondria takes center stage in the aging process.

The problem isn't so much that mitochondria become dysfunctional; this happens all the time in normal/healthy cells, but when it does, they are repaired or replaced. During aging, mitochondrial quality control pathways that gobble up damaged mitochondria and replace them with new, fresh ones are diminished. The accumulation of damaged, dysfunctional mitochondria compromises energy production and can trigger inflammation^[14] via specialized intracellular complexes called inflammasomes.^[14] Once activated, inflammasomes cause cells to send out danger signals in the form of pro-inflammatory cytokines, such as IL-1 β .^[14]

Animal models have shown that [aerobic exercise](#) in mice^[15] and alternate-day fasting in rats^[16] can improve healthspan by activating mitochondrial quality-control mechanisms. The good news is that all indications point to the same thing occurring in humans, through common mechanisms.^[17] So we may have some say in whether or how mitochondrial issues arise later in life.

Loss of proteostasis

Proteostasis is like quality control for the proteins in our cells. Most of the countless chemical reactions in the body at any instant are catalyzed by enzymes made of protein. These enzymes — or any protein, for that matter — need to be in a specific conformation to do their job. Structure is in part determined by the order of amino acids, but this is not enough. In addition to having the correct primary sequence, the protein needs to be folded into the right conformation. If misfolded, it might not be able to do its job, and the

problems don't stop there.

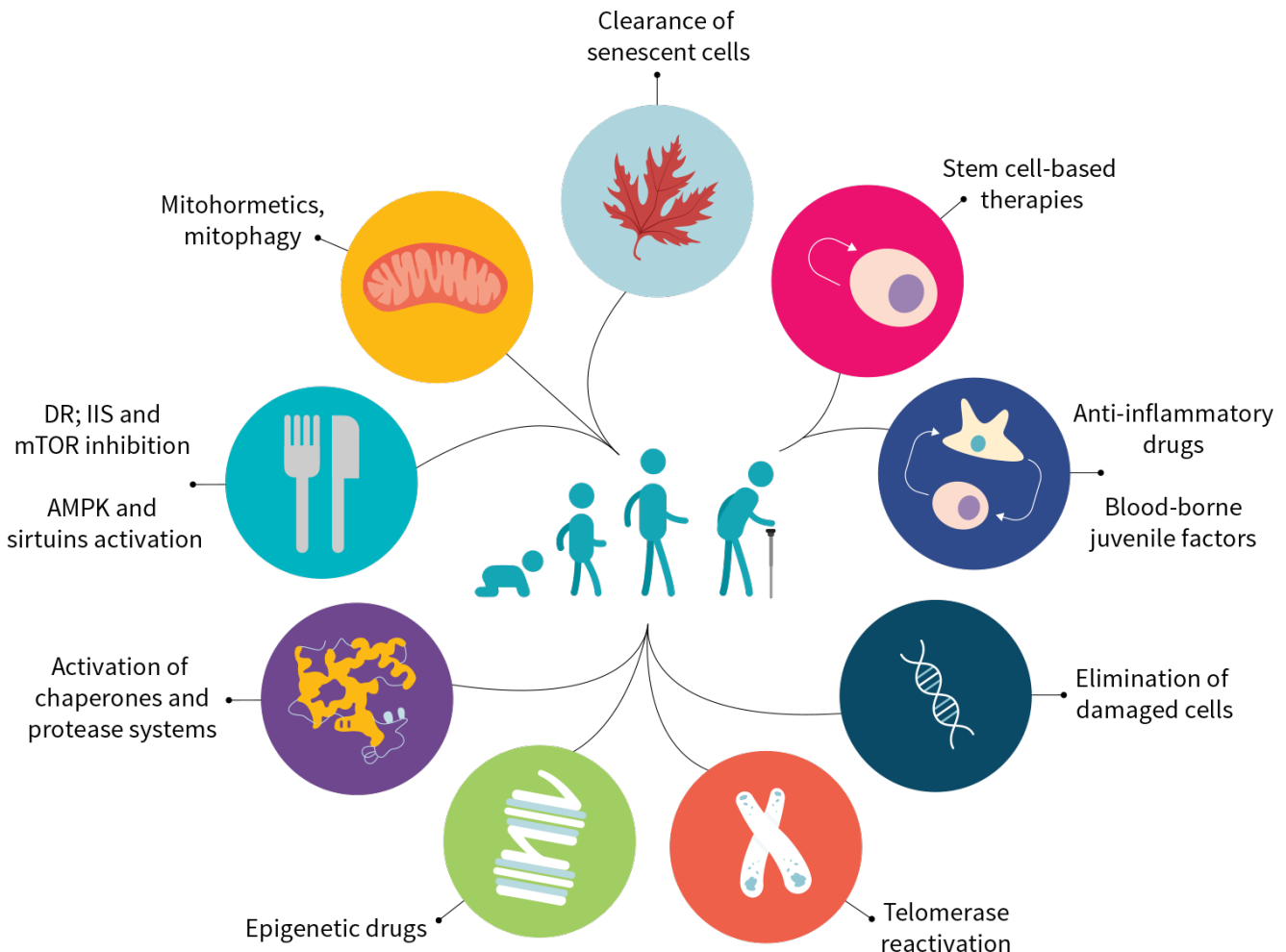
Individual amino acids tend to have different charges; some are quite soluble, while others are not. For this reason, hydrophobic amino acids (those that repel water) tend to be buried inside the larger structure of the protein. If the protein is misfolded, not only does it become less soluble or totally insoluble, but it also tends to become stickier, forming disorganized aggregates that are toxic to the cell. The ability to maintain proteostasis decreases with age and is behind many of the neurodegenerative diseases associated with protein aggregation,^[19] such as Alzheimer's, Parkinson's, Huntington's, and others. The accumulation of misfolded, toxic proteins triggers an inflammatory response, also contributing to increased inflammation during aging.

There are two defense mechanisms against this accumulation, and both have been shown to become compromised over time during the aging process. Chaperone proteins assist with folding new proteins as they are synthesized,^[19] and their levels are increased by stress, such as the type that occurs during exercise.^[20] On the other hand, proteolytic systems, such as autophagy,^[21] are tasked with breaking down toxic aggregates after they've formed.

So far we've covered some of the major mechanisms that drive the aging process. The list is far from exhaustive, but by now you get the picture. A decline occurs at a number of levels, in a number of systems, which ultimately shortens healthspan and lifespan.

The [core supplements](#) we've outlined in this guide are a great place to start. They have solid track records, backed up by robust research, and you can't go wrong with them. In addition to supplementation, there are also some "core actions" you can take to encourage a longer healthspan (and perhaps lifespan).

Therapeutic interventions that might extend healthspan



Strategies for healthy aging

Get moving

Present-day humans tend to move too little and eat too much, and this is a potent negative combination. We simply are not designed to be sedentary, nor were we likely designed for the level of excess in the typical Western diet. Granted, some of this is out of our control. Many of us have desk jobs during the day and then family responsibilities at night. That being said, we need to find a way. Park the car in the back of the parking lot if necessary. Take the stairs instead of the elevator. Get in a quick 30-minute workout before work. The small investment in time now could pay big dividends down the road and put you on a trajectory to being fit and high functioning well into your later years.

People who stick to solid fitness programs tend to look younger at any age. The evidence is not just anecdotal; exercise has been shown to lessen many of the hallmarks of aging.^[22] And it does this by affecting multiple body systems in a positive way. So get moving!

Already on solid footing from a diet and exercise standpoint? Here are some additional things to consider.

Train hard but smart

As you transition from your 30s to your 40s, some things will change. First, certain hormones start to trend downward, which can increase the time needed for full recovery after an intense training session. Also, many years of hard training can increase the efficiency with which your nervous system recruits motor units during heavy lifts. In other words, your ability to do damage to a muscle during a training session could edge out your ability to recover from that session in a timely fashion. This can also leave you more susceptible to injury, especially when you're unaccustomed to an exercise.

I have personal experience with this. When I was 36, I decided that I hadn't done enough HIIT (high-intensity interval training) lately — it had been a couple of years, at least — as most of my cardio at the time was mountain biking. I was in good shape, and also weight-training four times a week, so I figured my physical condition was fine to jump right into some hill sprints. About midway through my second sprint — with little warm-up — I felt a slight twinge in my left calf. It was something in between a cramp and a spasm, but not so bad that I felt I had to stop. This, it turns out, was an unheeded warning sign. On the next sprint, about halfway up the hill, I heard and felt a loud pop in my left calf muscle, followed by intense pain and loss of strength. I had a partial tear in my gastrocnemius muscle, which totally caught me by surprise. I thought to myself, *I'm in good shape. How could this happen?* It turns out this is common in athletes over 30. We still feel like we are in our 20s and fail to recognize the need to adjust until an injury seems to fall out of the sky.

Of course, hindsight is 20/20. It's still important to learn from mistakes though. Even better, learn from the mistakes of others. You can learn the following from mine:

- Warm up habitually and more than you think you need to. (You heard me, people over 30!)
- Introduce new exercises with caution
- Listen to your body. If it feels off, it probably is. Don't be afraid to make adjustments

Mobility

Most people, especially those of us who need to sit for a significant portion of the workday, will suffer from a progressive loss of mobility with age. Muscles and joints become tighter, and range of motion is lost, which partly explains the increased incidence of lower back pain with aging.^[23]

In the past, the only time mobility and stretching came into the picture for me was after I was forced to deal with an injury. This, of course, was a mistake, because diligent focus on the mobility issues I was having at the time may have prevented injury in the first place. I was strong in my 20s and early 30s on compound exercises, such as deadlifts and squats. I continued to increase my strength during my early 30s but started to develop more frequent setbacks, due to the increasing fragility of my lower back. I would have a great training session, and then 4–5 days later, my back would go out after doing some random low-intensity activity like picking something up off the floor.

Of course, once injured, I would start stretching and doing mobility work to restore function. But I had it backward. It was the underlying mobility issues that were causing my problems in the first place. The stronger I got, the more they reared their ugly head.

I fixed the issue with a drastic change in my approach to training. A lack of hip mobility was precipitating most of the issues with my lower back. For some time, I replaced workouts with stretching and mobility sessions to address these weak points. I then continued to work on mobility but phased in weight training, but with a focus on core strength and posterior chain. The end result? My bench press sure didn't increase, but my lower back is no longer fragile, nor am I limited in terms of exercise. (Before my mobility reboot, I had to eliminate squats and deadlifts completely from my training.)

- Expect mobility issues to come up with increasing age, and be proactive about addressing them.
- To avoid trial, error, injuries, and lost time, seek a qualified fitness or medical professional to address mobility issues before they lead to injury or loss of function.

Sleep and recovery

Most of us are not getting as much sleep as we need. This is self-evident, more or less. We all recognize the brain fog, irritability, and fatigue that come with several days' worth of inadequate sleep. The more insidious fallout is that sleep deprivation may even accelerate aging at the cellular level.^[24] The solution is to get as much rest as *you need*. Not everybody needs 8 hours of sleep; some can get by with less, but some of us need even more. Of course, this isn't always an option. When you are pushing hard with your job or have young children — or both — sleep becomes a precious commodity.

The solution is to get as much sleep as you need as consistently as you can.

Recommended hours of sleep

AGE	RECOMMENDED	MAY BE APPROPRIATE	NOT RECOMMENDED
0–3 months	14–17	11–19	<11 or >19
4–11 months	12–15	10–18	<10 or >18
1–2 years	11–14	9–16	<9 or >16
3–5 years	10–13	8–14	<8 or >14

AGE	RECOMMENDED	MAY BE APPROPRIATE	NOT RECOMMENDED
6–13 years	9–11	7–12	<7 or >12
14–17 years	8–10	7–11	<7 or >11
18–25 years	7–9	6–11	<6 or >11
26–64 years	7–9	6–10	<6 or >10
≥65 years	7–8	5–9	<5 or >9

Adapted from Hirshkowitz. *Sleep Health*. 2015.^[25]

Eat a healthy diet and maintain a healthy weight

Poor nutrition, excess calorie intake, and the resulting weight gain — and possibly obesity — are at odds with a long lifespan and healthspan. Most know this, but recognizing you are overweight is far easier than sustainably addressing it. Nobody gets out of shape on purpose; it creeps up on us. Even if you could eat whatever you wanted in your 20s and still look like a superhero, odds are it'll be harder to pull off in your 30s and unlikely to impossible in your 40s and later.

And this is how most of us trend toward negative changes in body composition over the years.^[26] But this doesn't have to be the case. Pay attention to changes in your body and how it responds to training, diet, and supplementation over time, and adjust accordingly.



*Bill Willis, senior researcher
PhD in Biomedical Science*

Combos

Core Combo

Vitamin B12

Each day, take 100–400 mcg of [vitamin B₁₂](#).

Blueberries

Each day, take [blueberries](#) according to one of the following protocols:

- Blueberry anthocyanins: 0.5–1 gram (500–1,000 mg)
- Blueberry powder: 12 grams
- Freeze-dried blueberries: 24 grams
- Fresh blueberries: 60–120 grams
- Pure blueberry juice: 500 mL (17 oz)

Carnitine


Twice a day, take 250–500 mg of [ALCAR](#) (i.e., 500–1,000 mg/day).

Protein

Consume protein throughout the day (1.0–2.2 grams per kilogram of body weight, so 0.45–1.00 g/lb), with the help of a protein powder if necessary. Consult the [protein](#) entry to set the intake level best suited to your needs.

Vitamin D

If your [25\(OHD\)](#) levels are adequate or you don't know your levels, 400 IU (10 mcg) of [vitamin D₃](#) per day may help maintain your levels in the adequate range. If your 25(OH)D levels are low, 800–2,000 IU (20–50 mcg) of D₃ per day is likely to raise them to an adequate level, at which point 400–1,000 IU (10–25 mcg) per day should suffice for maintenance. In case of full-blown deficiency, a medically supervised intervention will be needed.

 **Tip: Try one combo alone for a few weeks**

Taking too many supplements at once may prevent you from determining which ones are truly working. Start with just one of the combos suggested here for a couple of weeks before you consider making any modification, such as adding another supplement, altering a supplement's dosage, or incorporating the supplements from an additional combo.

When adding another supplement to your regimen, be methodical. For example, you may wish to take all the supplements from two combos. Select the combo that you wish to try first and take this for a couple of weeks. Then, add one supplement from the second combo and wait another week to see how it affects you. Continue this process until you've added all the supplements you wish to.

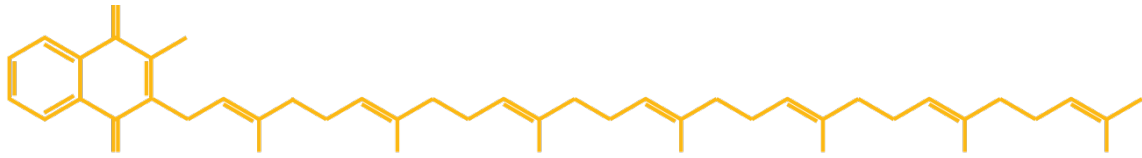
If a supplement appears in two combos you wish to combine, don't stack the doses; instead, combine the ranges. For instance, if the range is 2–4 mg in one combo and 3–6 mg in the other, your new range becomes 2–6 mg. Always start with the lower end of the range — especially in this case, since the reason why one of the ranges has a lower ceiling in one combo may be due to a synergy with another supplement in the same combo. Reading through the full supplement entry may help you decide which dose to aim for, but if you're not sure, lower is usually safer.

Specialized Combos

Bone health

Each day, take 3–5 grams of [creatine monohydrate](#), 200 mg of [magnesium](#), and some [vitamin-k](#)|vitamin K]: 200 mcg (0.2 mg) of *MK-7* and/or 45,000 mcg (45 mg) of *MK-4*.

Vitamins that increase bone mineralization

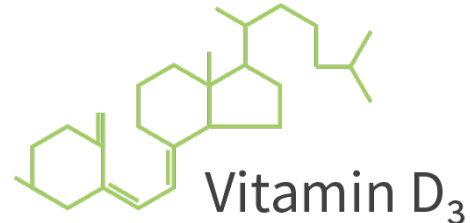


Vitamin K₂ MK-4

Can reduce the risk of arterial calcification.

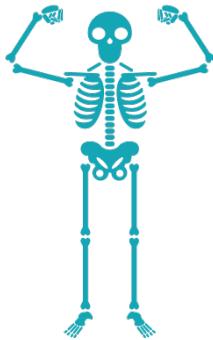


Increase separately and synergistically the rate at which minerals (notably calcium and magnesium) accumulate in bones.



Vitamin D₃

Helps the intestines absorb calcium.



Cardiovascular health

Each day, take 3–5 grams of [creatine monohydrate](#), 200 mg of [magnesium](#), and some [vitamin-k](#)|vitamin K]: 200 mcg (0.2 mg) of *MK-7* and/or 45,000 mcg (45 mg) of *MK-4*.

Each day, take [L-carnitine](#). Have you suffered from cardiovascular complications?

- *Yes*: take 2–9 grams.
- *No*: take 0.5–2 grams (500–2,000 mg).

Cognition

Each day, take 3–5 grams of [creatine monohydrate](#).

Twice a day, take 250–1,000 mg of [CDP-choline](#) (i.e., 500–2,000 mg/day) and 500 mg of [ALCAR](#) (i.e., 1,000 mg/day), preferably without food. This ALCAR dosage replaces the one in the [core combo](#).

Energy and stamina

Each day, take 3–5 grams of [creatine monohydrate](#) and 200 mg of [magnesium](#).

If your [DHEA-S](#) levels are low, take 20–50 mg (males) or 10–30 mg (females) of [DHEA](#) per day. Ideally,

supplement at the low end of the range for a month then get tested again.

Immunity

If you are underconsuming [vitamin E](#) or have [low blood levels](#), take 200 IU (134 mg of natural α -tocopherol or 90 mg of synthetic α -tocopherol) per day. Since vitamin E has anticoagulant properties, make sure your diet contains at least your Adequate Intake (AI) of [vitamin K](#) (90 mcg/day for female; 120 mcg/day for males).

Libido

Take [maca](#) (2–3 g) at breakfast.

If your [DHEA-S](#) levels are low, take 20–50 mg (males) or 10–30 mg (females) of [DHEA](#) per day. Ideally, supplement at the low end of the range for a month then get tested again.

Symptoms of menopause

Take [maca](#) (2–3.5) at breakfast.

Primary Supplements

Blueberries

What makes *blueberries* a primary supplement

The [anthocyanins](#) and [pterostilbene](#) in blueberries can help protect the brain and reduce [cognitive decline](#).^[27] Episodic memory and executive function are most likely to benefit — the former especially in adults with mild cognitive impairment. Working memory might benefit too, but the evidence is mixed.

Anthocyanins are also the probable reason why blueberries can increase the activity of [neuronal growth factor](#) (NGF), a protein that acts as a neurotransmitter. NGF helps neurons grow, branch toward each other, and thus communicate better. In seniors, a diet high in blueberries can improve [cognitive ability](#) in as little as six weeks.^{[28][29][30][31][32]}

On average, 100 grams of fresh blueberries contains 200 mg of anthocyanins^[33] and 4 mcg (0.004 mg, or 4,000 ng) of pterostilbene,^{[34][35][36]} but actual contents depend on variety, soil, season, weather, farming method, shipping time, storage conditions, and storage duration.

Nanograms (ng) of pterostilbene per gram (g) of blueberry (dry mass)

STUDY	SAMPLES	CULTIVARS	RANGE	AVERAGE
2011	6	1	—	11
2005	17	9	12–274	54
2004	3	2	9.9–52	26

References: Rodríguez-Bonilla et al. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2011.^[34] ● Rimando and Barney. *Acta Horti.* 2005. DOI:[10.17660/ActaHortic.2005.680.20](https://doi.org/10.17660/ActaHortic.2005.680.20) ● Rimando et al. *J Agric Food Chem.* 2004. DOI:[10.1021/jf040095e](https://doi.org/10.1021/jf040095e)

Warnings about *blueberries*


Blueberries are not known to interact negatively with any supplements or pharmaceuticals. However, anthocyanins and pterostilbene are both mildly hypoglycemic, so it is theoretically possible (though not probable) for the blueberry doses listed below to cause low blood sugar (i.e., [hypoglycemia](#)) when taken with other supplements or pharmaceuticals that can lower blood sugar, such as most [diabetes medicines](#).

How to take *blueberries*

Studies support the following protocols:

- Blueberry anthocyanins: 0.5–1 g/day
- Blueberry powder: 12 g/day
- Freeze-dried blueberries: 24 g/day

- Fresh blueberries: 60–120 g/day
- Pure blueberry juice: 500 mL/day (17 oz/day). Cheaper “blueberry juices” made with artificial flavoring and added sugar more than with actual blueberries will have little to no anthocyanins. Be sure to check the ingredients label.

 **Tip: Why don't you recommend brands or specific products?**

For two reasons:

- We don't test physical products. What our researchers do — all day, every day — is analyze peer-reviewed studies on supplements and nutrition.
- We go to great lengths to protect our integrity. As you've probably noticed, we don't sell supplements, or even show ads from supplement companies, even though either option would generate a lot more money than our Supplement Guides ever will — and for a lot less work, too.

If we recommended any brands or specific products, our integrity would be called into question, so ... we can't do it. That being said, in the interest of keeping you safe, we drew [a short list of steps you should take](#) if a product has caught your interest.

Carnitine

What makes *carnitine* a primary supplement

Carnitine plays a role in [cognition](#),^[37] energy metabolism,^[38] and [cardiovascular health](#).^{[39][40][41]} Though your body can synthesize it out of [lysine](#) and methionine, two amino acids, nearly three-fourths of the carnitine in omnivorous people comes from the meat, fish, eggs, and dairy products they consume.

Selected food sources of carnitine

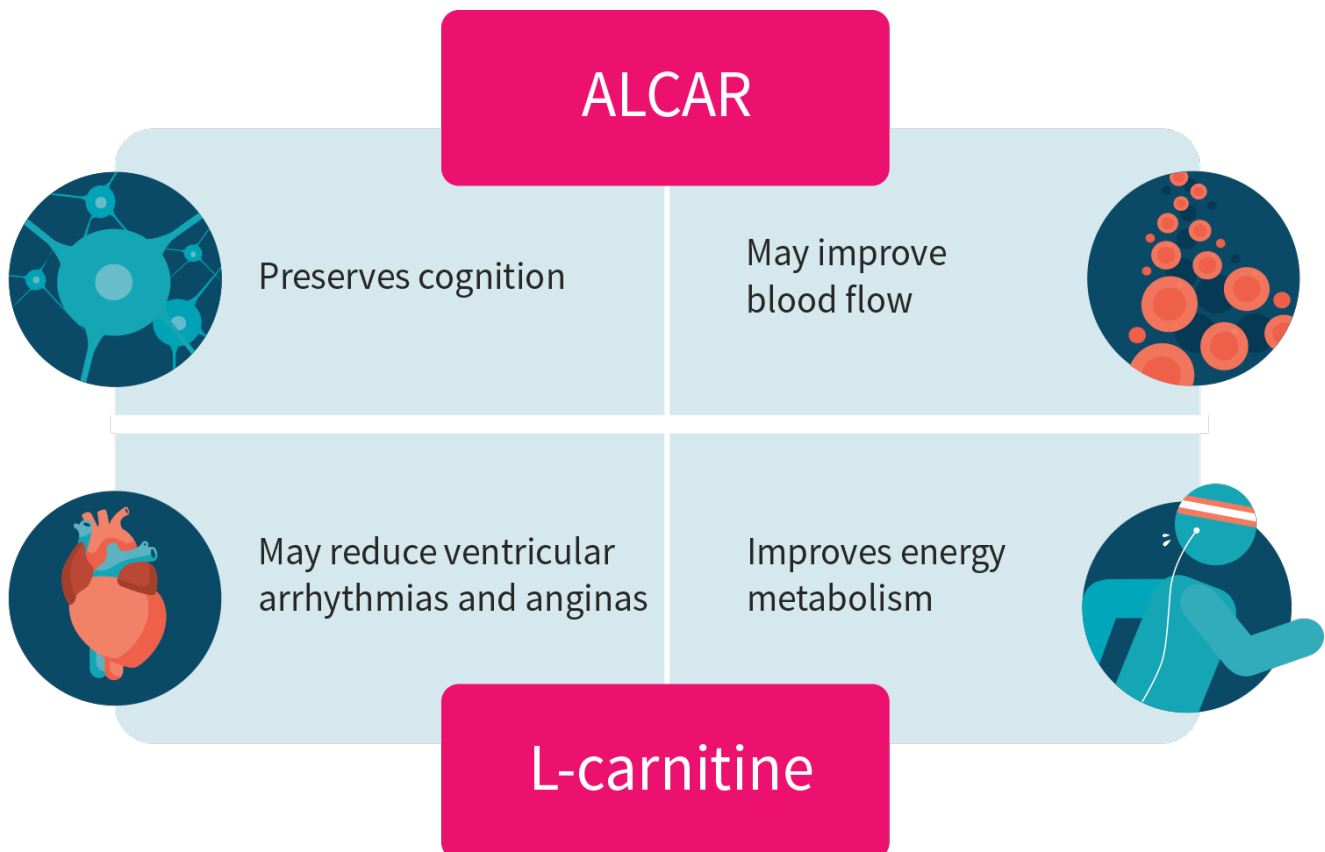
FOOD	PORTION	MILLIGRAMS (mg)
Beefsteak, cooked	4 oz	56–162
Ground beef, cooked	4 oz	87–99
Whole milk	1 cup	8
Codfish, cooked	4 oz	4–7
Chicken breast, cooked	4 oz	3–5
Ice cream	½ cup	3
Cheddar cheese	2 oz	2
Whole-wheat bread	2 slices	0.2
Asparagus, cooked	½ cup	0.1

Your body's ability to synthesize carnitine decreases as you age. In seniors, carnitine supplementation may reduce muscular fatigue, and preliminary evidence suggests that it may improve muscular control.

Also, people who have suffered a heart attack can supplement carnitine as an add-on treatment to possibly lower the risk of both abnormal heartbeats in the lower chambers (i.e., ventricular [arrhythmia](#)) and pain in the chest or limbs caused by poor blood circulation (i.e., [angina](#)).^[42]

Finally, a form of carnitine known as *acetyl-L-carnitine* (ALCAR) may benefit cognition by improving blood flow and promoting efficient energy use in brain cells.

Summary of carnitine's benefits



Warnings about *carnitine*

Side effects are generally rare, but some cases of upset stomachs have been reported. Higher doses of L-carnitine (2 g/day or more) can be converted into the compound trimethylamine, which in *some* people can give a fishy odor to urine, sweat, or breath.

Carnitine and its derivatives might interact negatively with some pharmaceuticals, including anticoagulants (such as warfarin/Coumadin and acenocoumarol/Sintrom). People on thyroid medication or with [hypothyroidism](#) may also wish to forgo carnitine, as it might depress thyroid hormone levels.

How to take *carnitine*

For neurological benefits, take *acetyl-L-carnitine* (ALCAR). Start with 250 mg twice a day (i.e., 500 mg/day). Over the course of a week, increase to 500 mg twice a day (i.e., 1 g/day). Taking ALCAR on an

empty stomach will result in more potent cognitive benefits. This type of carnitine has a tart taste, but it can be dissolved in tea or coffee and still retain its effects.

For general non-neurological benefits, take 2 grams of *L-carnitine* per day, with carbohydrates if you wish to increase the rate of absorption by the muscles.

In people at risk but who have not yet suffered cardiovascular complications, 500–2,000 mg of *L-carnitine* per day might offer some protection when taken in conjunction with prescribed medical therapies. People who have already suffered a heart attack, however, would need *at least* 2,000 mg (i.e., 2 g) and preferably 5,000–9,000 mg (i.e., 5–9 g) to see a reduction in arrhythmia, angina, and all-cause mortality.

L-carnitine can also be consumed as *L-carnitine L-tartrate* (LCLT) or *glycine propionyl-L-carnitine* (GPLC). You can supplement 500–2,000 mg of L-carnitine through 750–3,000 mg of LCLT or GPLC. You can supplement 5,000–9,000 mg of L-carnitine through 7,500–13,500 mg of LCLT or GPLC. However, neither LCLT nor GPLC has proven advantages over regular L-carnitine, both are more expensive, and GPLC also clumps easily in moist environments.

Protein

What makes *protein* a primary supplement

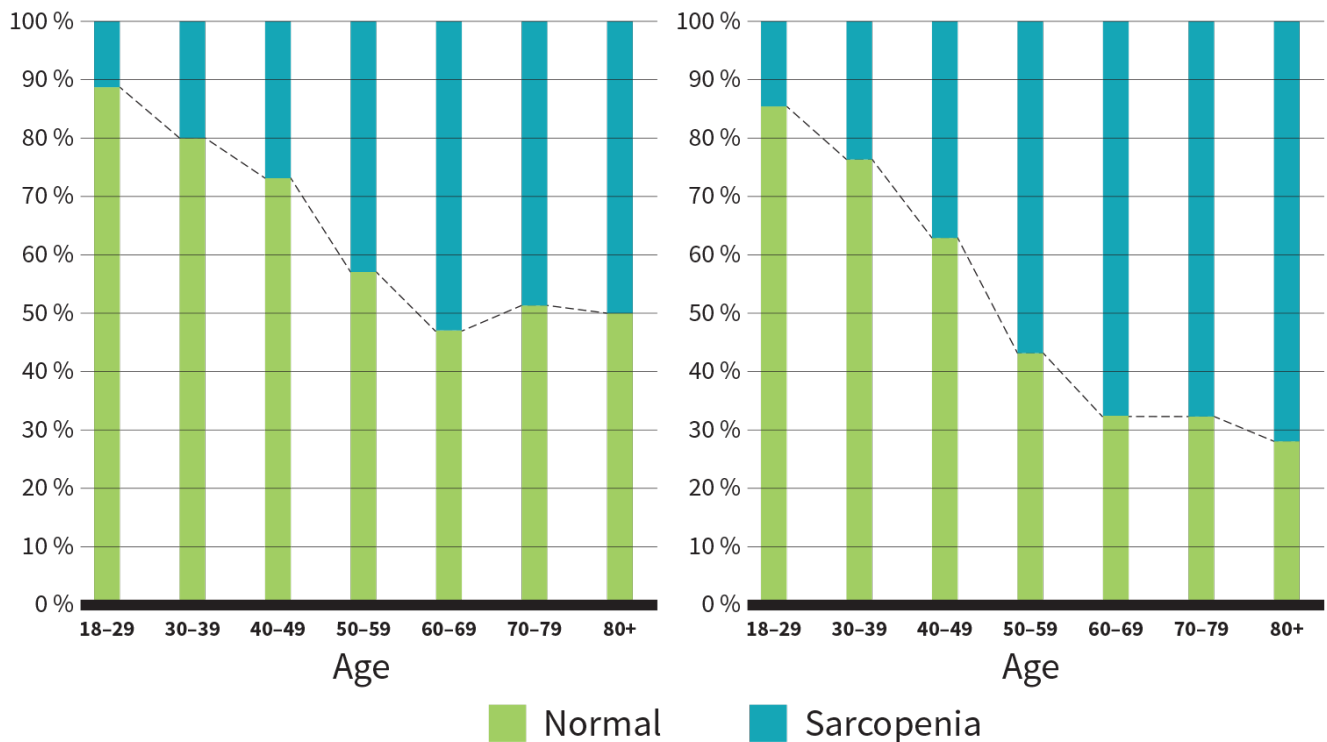
Dietary protein (the protein you ingest) plays important roles in your body, notably as a provider of *essential amino acids* (EAAs), the amino acids your body needs but cannot synthesize. In seniors, higher protein intakes are associated with greater [muscle mass](#), and greater muscle mass with greater [longevity](#) and [bone mineral density](#).^{[43][44][45]}

Age-related muscle loss, also known as *sarcopenia*, affects about 50% of males and 70% of females past the age of sixty, but it can start as early as your twenties.^[46]

Prevalence of sarcopenia by age and sex in the US

PREVALENCE IN MALES

PREVALENCE IN FEMALES

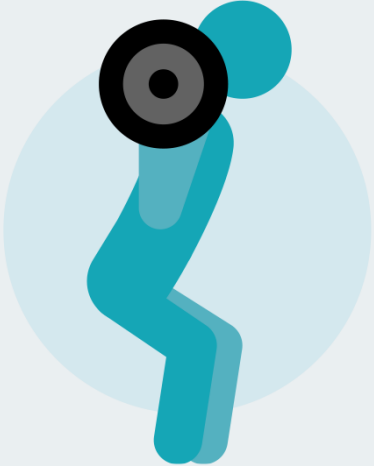



Reference: Janssen et al. *J Am Geriatr Soc.* 2002.^[46]

Fortunately, sarcopenia is neither inevitable nor irreversible — some seniors have built more muscle in their old age than they ever had in their youth. The older you get, however, the greater your muscles' anabolic resistance (i.e., their resistance to growth),^[47] and so the greater the exercise volume and protein intake you'll need to stimulate *muscle protein synthesis* (MPS).^{[48][49]}

In other words, the older you get, the more exercise and protein you need in order to gain muscle. In fact, as you get older, *aerobic exercise* (aka "cardio") may no longer suffice to ward off sarcopenia; you'll need to include *resistance training* to your routine.^[48]

A basic resistance training program for seniors

CONVENTIONAL RESISTANCE TRAINING	BODYWEIGHT RESISTANCE TRAINING
	
<p>Exercise at least twice a week.</p> <p>Train your whole body.</p> <p>Progressively increase the weight, reps, and/or sets.</p> <p>For each exercise, use 30–70% of the maximum weight with which you're able to perform at least one rep.</p> <p>Perform 2–3 sets of 6–15 reps or 1–2 sets of as many reps as possible (at least 14).</p>	<p>Exercise at least twice a week.</p> <p>Train your whole body.</p> <p>Progressively increase the reps and/or sets.</p> <p>Perform 1–3 sets of as many reps as possible.</p>

Adapted from Mcleod et al. *Front Physiol.* 2019.^[48]

As you get older, you may also need to increase your protein intake, as described [below](#). Overall, [whole foods](#) are the healthier choice, but if your food intake does not cover your daily protein needs, you could add a supplement (preferably a powder, since the protein-to-calorie ratio of powders tends to be higher than that of other protein supplements, such as protein bars).

[Whey protein](#) and [casein](#) powders are both derived from [milk protein](#) (which is 20% whey and 80% casein). Whey protein digests faster and has a higher concentration of EAAs (notably of [leucine](#), the most anabolic of the amino acids). It quickly increases EAA concentrations in the blood and is thus better able to stimulate MPS in anabolically resistant seniors.

[Whey protein concentrates](#) are the most common type of protein powder; they're inexpensive and mix easily, and so are probably your best option if you are not vegan. Look at the food label: your powder should be close to 80% protein. A little lower is fine if the powder is flavored (any flavoring will use a percentage of the powder), but any big discrepancy should steer you away.

But what if you *are* vegan? Fortunately, you can still supplement with protein powders. For vegans, two popular options are [soy protein](#), which is a complete protein, and a 70:30 pea:rice protein blend, whose amino acid profile is similar to that of whey protein.

Warnings about *protein*

Very high doses (at least 3 grams of protein by kilogram of body weight per day, so ≥ 1.36 g/lb/day), may cause gastrointestinal issues and increase your levels of [blood urea nitrogen](#) (BUN),^[50] a measure of kidney

function. High-protein diets also increase *glomerular filtration rate* (GFR), a marker for waste filtration in the kidneys,^[51] and it was once argued that increased GFR was a sign that undue stress was put on the kidneys,^[52] but later research has shown that [kidney damage does not occur as a result of diets high in protein](#).^{[53][54]}

By raising BUN and GFR, however, *high protein intakes may mask underlying issues*. Consider having your BUN and GFR levels tested before you start consuming a diet very high in protein, so as to both get a baseline measurement and check up on your kidney function. If you are already consuming ≥ 3 g/kg/day yet plan to have your BUN or GFR tested, lower your protein intake to ≤ 1.8 g/kg/day for at least 1 week prior to testing so as to prevent a false positive.

If you have *milk allergies*, you should avoid supplements that contain whey protein or casein (the two proteins in milk). The most notable alternatives are egg protein and the vegan options described in the last paragraph of the previous section.

If you are *lactose intolerant*, you have the same options as people with milk allergies, but you may also be fine with a whey protein concentrate, since most of the lactose has been removed. Whey protein isolates contain even less lactose, but never zero (in the United States, a powder can be labeled as “lactose-free” if it contains less than 0.5 grams of lactose per serving). If you wish to try an isolate, look at the food label: your powder should be close to 90% protein. A little lower is fine if the powder is flavored (any flavoring will use a percentage of the powder), but any big discrepancy should steer you away.

How to take *protein*

In the United States, the Recommended Dietary Allowance [RDA](#) of 0.8 grams per kilogram of body weight (0.36 g/lb) is considered the minimum amount of protein a healthy adult must consume daily to prevent muscle wasting when total caloric intake is sufficient.^[55]

The current evidence suggests, however, that this amount has been underestimated. Recent studies point to 1.0–1.2 g/kg as the minimum daily intake before the body starts downregulating important non-essential processes, from immune function to muscle protein synthesis.^{[56][57][58]} Even a reanalysis of the data used to establish the above RDA suggests the minimum daily intake should be at least 1.0 g/kg.^[59]

So, how much protein do you need daily?

- Sedentary but healthy seniors: 1.0–1.2 g/kg (0.45–0.54 g/lb)
- Sick or injured seniors: 1.2–1.5 g/kg (0.54–0.68 g/lb)
- Seniors wishing to lose weight: 1.5–2.2 g/kg (0.68–1.00 g/lb)
- Seniors wishing to build muscle: 1.7–2.0 g/kg (0.77–0.91 g/lb)

Daily protein intake

BODY WEIGHT	BODY WEIGHT	0.36	0.45	0.54	0.68	0.82	0.91	1.00	g/lb
LB	KG	0.8	1.0	1.2	1.5	1.8	2.0	2.2	g/kg
100	45	36	45	54	68	81	91	100	g
125	57	45	57	68	85	103	113	125	g
150	68	54	68	82	102	122	136	150	g

BODY WEIGHT	BODY WEIGHT	0.36	0.45	0.54	0.68	0.82	0.91	1.00	g/lb
LB	KG	0.8	1.0	1.2	1.5	1.8	2.0	2.2	g/kg
175	79	64	79	95	119	142	159	175	g
200	91	73	91	109	136	164	181	200	g
225	102	82	102	122	153	184	204	225	g
250	113	91	113	136	170	203	227	250	g
275	125	100	125	150	187	225	249	275	g

References: Schoenfeld and Aragon. *J Int Soc Sports Nutr.* 2018.^[60] ● Jäger et al. *J Int Soc Sports Nutr.* 2017.^[61] ● Thomas et al. *Med Sci Sports Exerc.* 2016.^[62]

Unless you have a [pre-existing condition](#) that affects your liver or kidneys, the intakes in the above table will not harm these organs.^[53] However, if you have a BMI of more than 30, you may want to calculate your protein requirements based on your goal body weight rather than your current body weight, so as to avoid overeating.

For maximal MPS stimulation, [the minimal per-meal dose of quality protein](#) (such as can be found in meat, eggs, dairy products, and soy) is 0.24–0.40 g/kg for adults in their twenties^{[49][63]} and 0.40–0.60 g/kg for adults aged sixty and older.^[49] Spreading your protein intake over a few meals, making sure this 0.40–0.60 g/kg threshold is met with each meal, will generally result in greater lean mass and strength.

Note that you don't need to calculate your intake so that it falls within the 0.40–0.60 g/kg range. This range isn't an ideal range — it is a range representing individual variations. In other words, some people can reach maximal MPS with just 0.40 g/kg, while others will need as much as 0.60 g/kg. Moreover, higher doses will not be wasted and are probably necessary when eating mixed meals that contain a variety of protein sources. You may have heard that if you eat more than 30 grams of protein in one sitting, the “excess” will pass undigested, but that's just a myth.

Desirable minimal protein intake range* per meal (g), by age for adults


BODY WEIGHT (lb)	BODY WEIGHT (kg)	20s	30s, 40s, 50s	≥60
100	45	11–18	13–24	18–27
125	57	14–23	17–30	23–34
175	79	19–32	23–43	32–48
200	91	22–36	27–48	36–54
225	102	24–41	30–54	41–61
250	113	27–45	33–60	45–68
275	125	30–50	37–67	50–75

* The ranges in this table represent individual variations. The minimum protein requirements increase as you age, but to what degree is uncertain because of the age gap left by the studies: most subjects were in their 20s (0.24–0.40 g/kg) or 60s/70s (0.40–0.60 g/kg). For people in their 30s, 40s, or 50s, the 0.29–0.53 g/kg range reflected in this table is an educated guess.

References: Schoenfeld and Aragon. *J Int Soc Sports Nutr.* 2018.^[60] ● Rafii et al. *J Nutr.* 2016.^[57] ● Morton et al. *Front Physiol.* 2015.^[63] ● Moore et al. *J Gerontol A Biol Sci Med Sci.* 2015.^[49] ● Rafii et al. *J Nutr.* 2015.^[56]

Your mileage may vary. The ranges in the paragraphs and table above cover the known extent of interindividual variations among healthy adults. However, as shown in the [“Prevalence of sarcopenia based on sex and age”](#) graphic, even people in their twenties can suffer from sarcopenia — in which case they would benefit from a protein intake closer to the one recommended in this table for adults over sixty.

After exercising, when your muscles are more sensitive to the anabolic effect of protein, take a dose in the range of your “desirable minimal protein intake per meal” (as shown in the table [above](#)). If you’ve been exercising on an empty stomach, you’ll be in negative protein balance, so take this dose as soon as possible. Otherwise, try to take it within a couple of hours — the exact size of your “window of opportunity” depends on how much protein you’re still digesting.^[64]

 **Tip: Use our Protein Intake Calculator**

Your protein needs hinge on many factors — notably your weight, health goals, and level of physical activity. Based on our research and the data you input, we can calculate your optimal daily protein intake. Click on the image below to get started!

**YOUR OPTIMAL
PROTEIN INTAKE:
???**

Vitamin B₁₂ (cobalamin)

What makes *vitamin B₁₂* a primary supplement

Suboptimal intake of vitamin B₁₂ (cobalamin) can cause [anemia](#), [cognitive impairment](#), [mood](#) disorders, nerve damage, and other health problems.^[65]

B₁₂ is present naturally only in animal products, so suboptimal intake is more common in vegetarians and vegans.^{[66][67]} Moreover, this protein-bound B₁₂ gets harder to digest as you age, so suboptimal intake is also more common in seniors.^[68] For those reasons, easily digestible B₁₂ is sometimes added to plant foods (which are said to be [fortified](#) with B₁₂).

Each vitamin has different forms, called vitamers. Four B₁₂ vitamers can be found in food.

- *Hydroxocobalamin*
- *Aquacobalamin*
- *Methylcobalamin*
- *Adenosylcobalamin*

Most supplements and fortified foods use the synthetic *cyanocobalamin*, which has the advantage of being particularly stable as long as it is kept away from bright light — *ultraviolet* (UV) rays in particular.^[69]

Warnings about *vitamin B₁₂*

People taking [metformin](#) may need to supplement B₁₂ or have their B₁₂ levels monitored, because this medicine may reduce B₁₂ absorption.^[70] However, people with kidney problems related to diabetes (i.e., [diabetic nephropathy](#)) should talk to their physician before supplementing B₁₂.^[71]

How to take *vitamin B₁₂*

All four commonly supplemented B₁₂ vitamers can degrade when exposed to UV rays,^[69] but *cyanocobalamin* and *hydroxocobalamin* are more stable (and widely available) than *methylcobalamin* and *adenosylcobalamin*.

Methylcobalamin and *adenosylcobalamin* can affect your body directly: they are *bioactive*. The other B₁₂ vitamers are not bioactive, but your body can transform them into *methylcobalamin*, which can be transformed into *adenosylcobalamin*. *Adenosylcobalamin* cannot be transformed into *methylcobalamin*, though, which is why it is seldom taken alone (it is usually paired with *methylcobalamin*).

Take *100–400 mcg/day* (all forms included). People on metformin or with absorption issues should aim toward the higher end of the range. People with swallowing difficulties or intestinal absorption issues can use sublingual B₁₂ supplements.

Fortunately, your body will not readily absorb more than it needs: doses as high as 1,000 mcg (1 mg) taken daily for 5 years have not been found to produce adverse effects.^[72] For that reason, even the Institute of Medicine (now known as the Health and Medicine Division) did not set a Tolerable Upper Intake Level (UL) for B₁₂.^[73]

Recommended Dietary Allowance (RDA) for vitamin B₁₂ (mcg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	0.4*	0.4*	—	—
7–12 months	0.5*	0.5*	—	—
1–3 years	0.9	0.9	—	—
4–8 years	1.2	1.2	—	—
9–13 years	1.8	1.8	—	—
>13 years	2.4	2.4	2.6	2.8

* Adequate Intake (AI)

Reference: Institute of Medicine. [Vitamin B₁₂](#) (chapter 9 of *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B₆, Folate, Vitamin B₁₂, Pantothenic Acid, Biotin, and Choline*. The National Academies Press. 1998. DOI:[10.17226/6015](#))

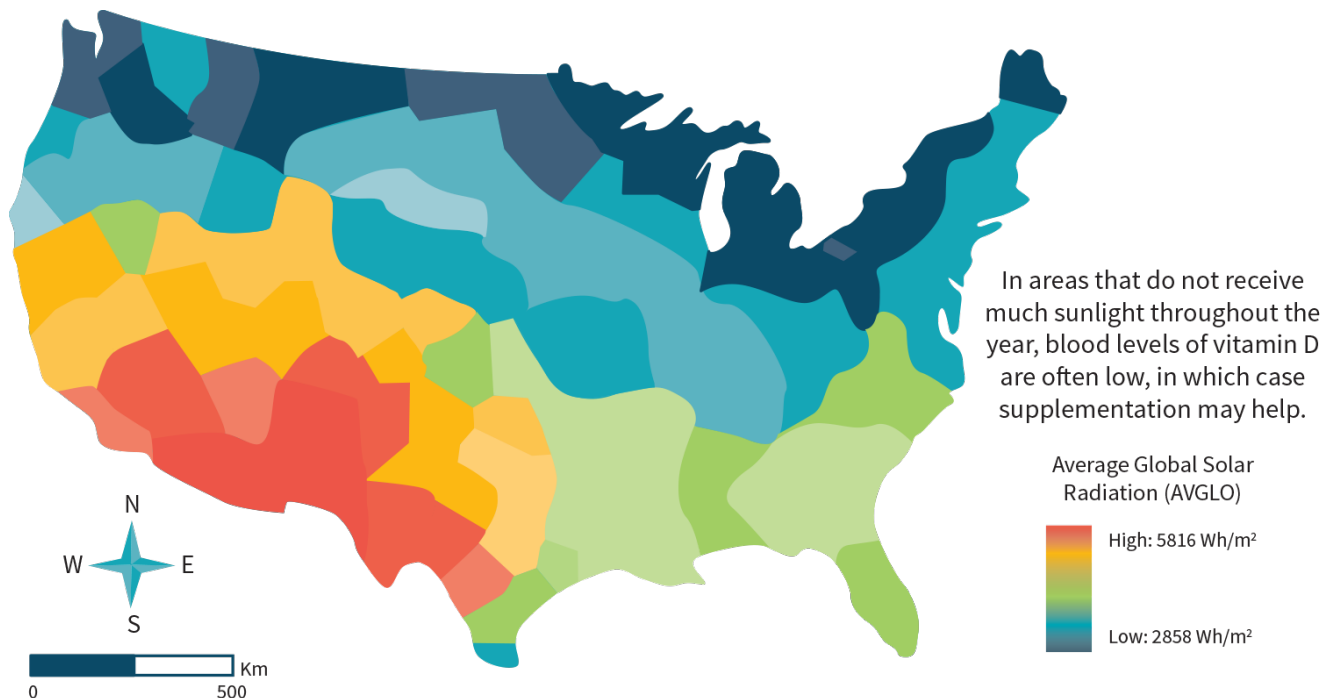
Vitamin D

What makes *vitamin D* a primary supplement

Suboptimal levels of vitamin D are common, especially in people whose skin exposure to sunlight (meaning without protection from clothes or sunscreen) is limited. Moreover, the darker your skin, the longer you need to expose yourself to sunlight to synthesize enough vitamin D, which is why people with darker skin are at an increased risk of suboptimal vitamin D levels.^[74]

The situation doesn't improve as you age. The older you get, the less efficient your body becomes at synthesizing vitamin D, the less time you're likely to spend outside, the less vitamin D you're likely to get through food, and the more likely you become to carry extra fat (belly fat has been linked to vitamin D deficiency).^{[75][76]}

Average yearly sunlight exposure in the US



Adapted from Tatalovich et al. *CaGIS*. 2006. DOI:[10.1559/152304006779077318](https://doi.org/10.1559/152304006779077318)

Vitamin D is commonly available in two forms. *Ergocalciferol* (D₂) is available in a handful of plants and fungi, whose D₂ content can be increased dramatically when exposed to *ultraviolet B* (UVB) radiation,^{[77][78]} whereas *cholecalciferol* (D₃) is synthesized from the cholesterol in your skin when exposed to the sun's UVB rays.^{[79][80][81]}

Before turning to supplementation, you should try incorporating some [foods rich in vitamin D](#) into your diet. Very few foods, alas, contain appreciable amounts of naturally occurring vitamin D, with fatty fish being a notable exception (cod liver oil, in particular). For that reason, milk is commonly fortified with either D₂ or, more recently, D₃. Why milk? Because milk is rich in [calcium](#), which vitamin D helps your intestines absorb. For the same reason, yogurt, cheese, and breakfast cereal are also commonly fortified with D₂ or D₃. Other commonly fortified foods include bread, margarine, and fruit juice (orange juice, in particular). As usual, which foods get fortified, if any, vary by country, based on local laws and policies.

By helping your intestines absorb calcium, vitamin D can strengthen your bones. Consuming large doses regularly can also facilitate the calcification of your arteries, unfortunately, but this effect may be counteracted by [vitamin K](#). Vitamins D and K may increase synergistically the rate at which minerals (notably calcium and [magnesium](#)) accumulate in bones, which is another reason to take them together.

Vitamin D supplementation might reduce the [risk of falls and fractures](#) in older people^[82] — though high single monthly doses ($\geq 24,000$ IU) taken for a year or more might increase the risk of falls.^[83] There is also observational evidence linking low levels of vitamin D with osteoporosis and other age-related diseases, such as cancer, hypertension, [cardiovascular disease](#), [type 2 diabetes](#), [cognitive decline](#), and [depression](#).^[75]

Vitamin D₃ is both more stable and more bioavailable than vitamin D₂. As a supplement, it is usually derived from lanolin^[84], a waxy substance secreted by the skin glands of woolly animals, but a vegan-friendly option (a lichen extract) is also available.

Warnings about *vitamin D*

Keep in mind that, over months, daily doses of 10,000 IU (250 mcg) or more can become toxic as well as lead to [hypercalcemia](#), a buildup of calcium in the soft tissues of the body (such as the arteries). The risk of hypercalcemia also increases when moderate doses of vitamin D (600–1,000 IU, so 15–25 mcg) are taken by people who also take high doses of [supplemental calcium](#). Likewise, the risk of [kidney stones](#) can increase when even modest doses of vitamin D (400 IU, so 10 mcg) are taken by people who also take high doses of [supplemental calcium](#).

If you supplement with more than 500 mg of calcium daily and this dose puts you over your RDA, consider reducing it before adding vitamin D. *Of course, if the calcium supplement you are taking was prescribed to you, consult the prescriber before making any changes.*

Recommended Dietary Allowance (RDAs) for calcium

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	200*	200*	—	—
7–12 months	260*	260*	—	—
1–3 years	700	700	—	—
4–8 years	1,000	1,000	—	—
9–13 years	1,300	1,300	—	—
14–18 years	1,300	1,300	1,300	1,300
19–30 years	1,000	1,000	1,000	1,000
31–50 years	1,000	1,000	1,000	1,000
51–70 years	1,000	1,200	—	—
>70 years	1,200	1,200	—	—

* Adequate intake (AI)

Reference: Institute of Medicine. *Dietary Reference Intakes for Calcium and Vitamin D*, table 5-1, [p. 349](#). The National Academies Press. 2011. DOI:[10.17226/13050](#)

If you take a [multivitamin](#), check to see if it contains vitamin D. It may already contain sufficient amounts

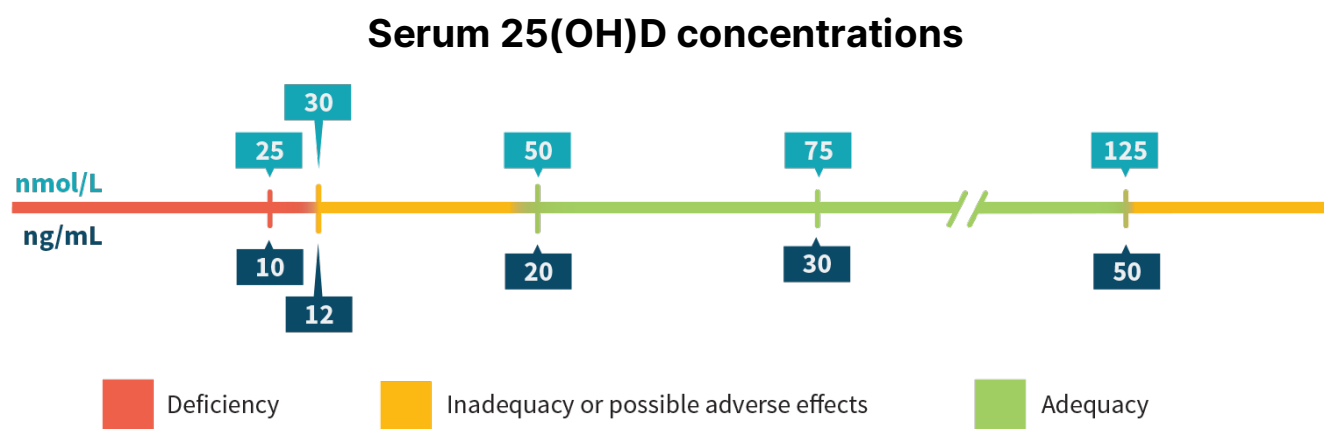
for your personal needs. Check the calcium dose as well, to ensure it is not too high.

A genetic mutation in the [CYP24A1](#) gene can cause [idiopathic infantile hypercalcemia](#).^[85] This condition, usually identified in childhood, causes high levels of calcium in the blood and urine and leads to calcium deposits in the kidneys. This mutation can lead to vitamin D toxicity with daily intakes as low as 500 IU (12.5 mcg).

[Orlistat](#) (Alli, Xenical) reduces how much fat you absorb from the food you eat. As a result, it also reduces the absorption of fat-soluble vitamins. If you take this medicine, take your vitamin D supplement at least 2 hours before or after.

How to take *vitamin D*

First, you should determine if you really need to supplement vitamin D by checking your current vitamin D levels — your [blood levels of 25-hydroxyvitamin D](#) (25(OH)D).



Reference: Institute of Medicine. [Overview of Vitamin D](#) (chapter 3 in *Dietary Reference Intakes for Calcium and Vitamin D*. The National Academies Press. 2011. DOI:[10.17226/13050](#))

In case of *deficiency*, a medically supervised intervention will be needed. *Do not begin any intervention without discussing it with your physician.* Common medical interventions include taking 50,000 IU (1,250 mcg) of D₂ or D₃ at least three times a week for six to eight weeks, though people with a borderline deficiency may not need as high a dose. At the end of this intervention, if vitamin D levels are above 30 nmol/L (12 ng/mL), a daily dose of 400–1,000 IU (20–25 mcg) is commonly used for maintenance.

In case of *inadequacy*, 800–2,000 IU (20–50 mcg) of D₃ per day is likely to raise vitamin D levels to an adequate level, at which point 400–1,000 IU (20–25 mcg) per day should suffice for maintenance.

In case of *adequate* vitamin D levels, a vitamin D supplement may not be necessary, especially if you spend a lot of time outside and live near the equator. However, taking 400–600 IU (10–15 mcg) of D₃ per day may help maintain vitamin D levels in the adequate range, particularly during the colder, darker months, when you are least likely to synthesize enough vitamin D from sun exposure.

In case of *high* vitamin D levels (which can cause adverse effects), seek the help of a medical professional. Of course, stop taking any supplement containing vitamin D, unless otherwise instructed by a medical professional.

If you do not know your vitamin D levels and cannot get them tested but are still intent on taking a vitamin D supplement, it would be prudent to limit yourself to a maintenance dose of 400 IU (10 mcg) of D₃ per

day. Alternatively, you could track your food intake for a week to determine your average vitamin D intake, then select a complementary dose to reach your RDA.

Recommended Dietary Allowance (RDAs) for vitamin D (IU*)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–12 months	400*	400*	—	—
1–13 years	600	600	—	—
14–18 years	600	600	600	600
19–50 years	600	600	600	600
51–70 years	600	600	—	—
>70 years	800	800	—	—

* 40 IU = 1 mcg

** Adequate intake (AI)

Reference: Institute of Medicine. *Dietary Reference Intakes for Calcium and Vitamin D*, table 5-3, p. 363. The National Academies Press. 2011. DOI:[10.17226/13050](https://doi.org/10.17226/13050)

If the maintenance doses in the paragraphs above prove insufficient, as could be the case notably if your BMI is over 30^[86] or if you suffer from poor vitamin D absorption or processing (due to a problem with your kidneys, liver, or gastrointestinal tract), you could switch to 1,000–2,000 IU (25–50 mcg) of D₃ per day.

Vitamin D being fat-soluble, it is better absorbed when taken with a fat-containing food or supplement (e.g., [fish oil](#)).

Secondary Supplements

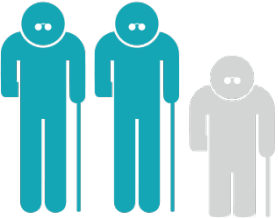
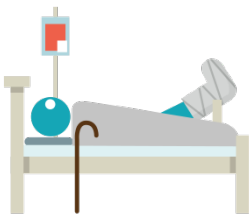

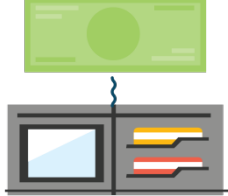
Creatine

What makes *creatine* a secondary option

Supplementing with creatine monohydrate increases the body's creatine stores, which are located primarily in the skeletal muscles.^[87] Your cells use creatine to regenerate *adenosine triphosphate* (ATP),^[87] life's energy currency, before they turn to burning glucose.

Creatine can improve muscular strength and control, and thus fitness and mobility.^[88] In seniors, these improvements might help reduce the risk of falls, though many more studies are needed for confirmation. When paired with resistance training, creatine may also improve bone health.^{[89][90]} When creatine levels are suboptimal, as is often the case in seniors, vegans, and vegetarians, taking creatine might also enhance cognition.^[91]

Seniors and the risk of falls

			
More than a third of older adults fall each year.	10% to 20% of falls cause serious injuries, such as fractures or the kind of head trauma that warrants hospital visits.	Non-fatal fall injuries are associated with decreased quality of life and loss of independence.	In the United States, direct medical costs for fall injuries amount to \$34 billion each year.

Reference: Steven et al. *Inj Prev*. 2006.^[92]

Warnings about *creatine*

Decades of research have demonstrated that creatine is generally well tolerated. The only recorded adverse effects are nausea, diarrhea, and stomach cramps in people taking more than 10 grams at once, and even at such high doses, these effects are rare.^[93] Still, should you find yourself particularly sensitive to creatine's digestive side-effects, split your daily dose, take it with some food, and drink more fluids. You could also try *micronized* creatine monohydrate, which dissolves more easily in liquids.

You may have heard that creatine can raise testosterone, the precursor to *dihydrotestosterone* (DHT), and can thereby accelerate or cause hair loss. To date, though, the overall body of evidence suggests that creatine doesn't affect testosterone or hair loss.^{[94][95][96][97][98][99][100][101][102][103][104][105]}

Creatine can cause water retention, which may notably increase body weight. This side effect is largely harmless and is reversed when creatine supplementation is stopped. Theoretically, this water retention

could harm people whose kidney disorder is being treated with [diuretics](#), which cause water loss.^[93] This possible harm is based on known mechanisms rather than human trial data.

Blood levels of creatine ([creatinine](#), a byproduct of energy production) are used as an indicator of [kidney function](#), but elevated levels caused by supplemental creatine are *not* a sign that your kidneys underperform.^{[106][107]} The current evidence does *not* support the persistent notion that creatine supplementation causes [kidney damage](#). In both long- and short-term studies, daily doses up to 10 grams were found *not* to impair kidney function in people with healthy kidneys.^{[93][108][109][110][111][112][113][114]} Daily doses above 10 grams too were found *not* to impair kidney function in people with healthy kidneys, but there are fewer long-term trials on such high doses.^[93]

Creatine's ability to raise creatinine levels may, however, mask underlying issues. Consider having your creatinine levels tested before you start taking creatine, so as to both get a baseline measurement and check up on your kidney function. If you are already taking creatine yet plan to have your creatinine tested, cease supplementation 3 weeks prior to testing so as to prevent a false positive.

Limited short-term evidence indicates that people with suboptimal kidney function may safely supplement with creatine. Long-term studies, however, are scarce.^{[115][116][117][118]} If your kidney function is suboptimal, you might wish to forgo creatine, or otherwise take only a low daily dose (such as 3 grams^[93]) after speaking with your physician. Out of caution, people taking medicines that increase the risk of harm or damage to the kidneys (i.e., [nephrotoxic drugs](#)) should skip creatine supplementation.

Finally, *do not buy liquid creatine products* — creatine breaks down into useless byproducts when left in liquids for too long.

How to take *creatine*

Take 3–5 grams of *creatine monohydrate* with food. [Other forms of creatine](#) may be more *expensive*, but studies have not found them to be more *effective*. People with more muscle mass may benefit from as much as 10 g/day, but this claim is not fully supported by the evidence. To supplement with 10 g/day, take 5 grams twice a day.

Loading creatine means taking a high daily dose for a few days (e.g., 25 g/day for 5 days) before moving down to a smaller maintenance dose, which can be taken indefinitely. This is not necessary for effective supplementation, however; benefits may be felt sooner through loading, but they normalize after a few weeks.

If you wish to load creatine, take 20–25 g/day for 7 days (you may help prevent intestinal discomfort by splitting your daily intake into smaller doses, taking them with some food, and drinking more fluids). Take 5 g/day thereafter.

Some people are creatine nonresponders: the creatine they ingest largely fails to reach their muscles.^{[119][120]} Note that even if supplemental creatine fails to enter your muscles it can still benefit you in other ways, such as by improving your body's methylation status (methylation being a way for your cells to help manage gene expression).

Alternate forms of creatine, such as creatine ethyl-ester, have been marketed to nonresponders, but they lack scientific support. Currently, the best way to lessen creatine nonresponse is to take 5 grams twice a day, each time with protein and carbs, preferably close to a time of muscle contraction (i.e., before or after your workout).

If you are *not* a creatine nonresponder, you need not worry about supplementation timing, though you should remember that taking your dose with food lowers the risk of an upset stomach.

Creatine can be added to any liquid, but it must be drunk within the day, because creatine in liquids degrades into creatinine over time (the higher the temperature and the lower the pH, the faster the degradation). If you add creatine to a hot liquid, increase your dose a little to compensate for potential degradation.

DHEA

What makes *DHEA* a secondary option

The hormone *dehydroepiandrosterone* (DHEA) circulates throughout your body and can be called on to make other hormones, notably [testosterone](#) and [estrogens](#).^[121] DHEA levels decrease with age, sometimes drastically; maintaining adequate DHEA levels can help support healthy testosterone levels), [libido](#), and [sexual function](#) in seniors.

Warnings about *DHEA*

If your hormone levels are healthy, supplementing with DHEA is unlikely to benefit you — don't play with your hormonal balance on a whim.

DHEA can mildly inhibit the activity of [CYP3A4](#), an enzyme that helps in the metabolism of a wide range of pharmaceuticals — from [antibiotics](#) to [blood pressure medicines](#). If you are currently on any medication, speak with your physician before taking DHEA.

A handful of trials reported an increase in [acne](#), particularly in females. People with acne, or a history of acne, may be more prone to this side effect.

Observational and mechanistic evidence suggests that *it may be prudent for people with a family history of prostate, ovarian, or breast cancer to avoid DHEA supplementation*, since it affects androgenic (testosterone, [DHT](#) ...) and estrogenic (estrogen, [progesterone](#) ...) hormones.

In some sports leagues, DHEA and its derivatives (such as [7-keto DHEA](#)) are banned substances; their use may result in suspension or expulsion from the sport. The legality of DHEA also differs by country and region: some regulate it as a supplement, others as a drug.

How to take *DHEA*

First, get tested. Your body synthesizes [DHEA sulfate](#) (DHEA-S) out of DHEA. Whereas blood levels of DHEA can change quickly, blood levels of DHEA-S are more stable. You want to know your DHEA-S levels.

Typical normal DHEA-S ranges (µg/dL / µmol/L)

AGE	MALES	FEMALES
18–19	108–441 / 2.92–11.91	145–395 / 3.92–10.66

AGE	MALES	FEMALES
20–29	280–640 / 7.56–17.28	65–380 / 1.75–10.26
30–39	120–520 / 3.24–14.04	45–270 / 1.22–7.29
40–49	95–530 / 2.56–14.31	32–240 / 0.86–6.48
50–59	70–310 / 1.89–8.37	26–200 / 0.70–5.40
60–69	42–290 / 1.13–7.83	13–130 / 0.35–3.51
>69	28–175 / 0.76–4.72	17–90 / 0.46–2.43

Reference: [DHEA-sulfate test](#). Medlineplus.gov. Last updated January 6, 2020; accessed February 6, 2020.

- If they are *normal*, you don't need to take DHEA.
- If they are *above normal*, do not take DHEA. Speak to your physician.
- If they are *below normal*, discuss taking DHEA with your physician.

If you decide to supplement, you can try taking DHEA once a day in the morning (with food) for a month, then get tested again.

- *Males* can take 20–50 mg/day.
- *Females* can take 10–30 mg/day.

These doses should suffice to maintain adequate circulating levels of DHEA. In cases of very low DHEA, 50 mg/day may be needed by both sexes.

Maca (for libido)

What makes *maca* a secondary option

Multiple studies show that maca, a root vegetable, enhances [libido](#) in older males and females. Libido may keep improving for up to 8 weeks before plateauing.^{[122][123]} It should be noted that maca has shown promise for postmenopausal females,^[124] an oft-overlooked population when it comes to libido enhancement.

Maca may serve to treat [sexual dysfunction](#) caused by *selective serotonin reuptake inhibitors* (SSRIs),^{[125][126]} a kind of [antidepressant](#). It can also mildly benefit males with erectile dysfunction from other causes.^[127]

Warnings about *maca*

Maca is not known to interact with any major hormones (such as [DHEA](#), [estrogen](#), or [testosterone](#)) or any pharmaceuticals. To date, however, research into maca's potential adverse effects is somewhat limited.

How to take *maca*

Take 2–3 grams of maca root powder at breakfast. For the purpose of improving libido, there is no

difference between red, black, and yellow maca.^[122]

Magnesium

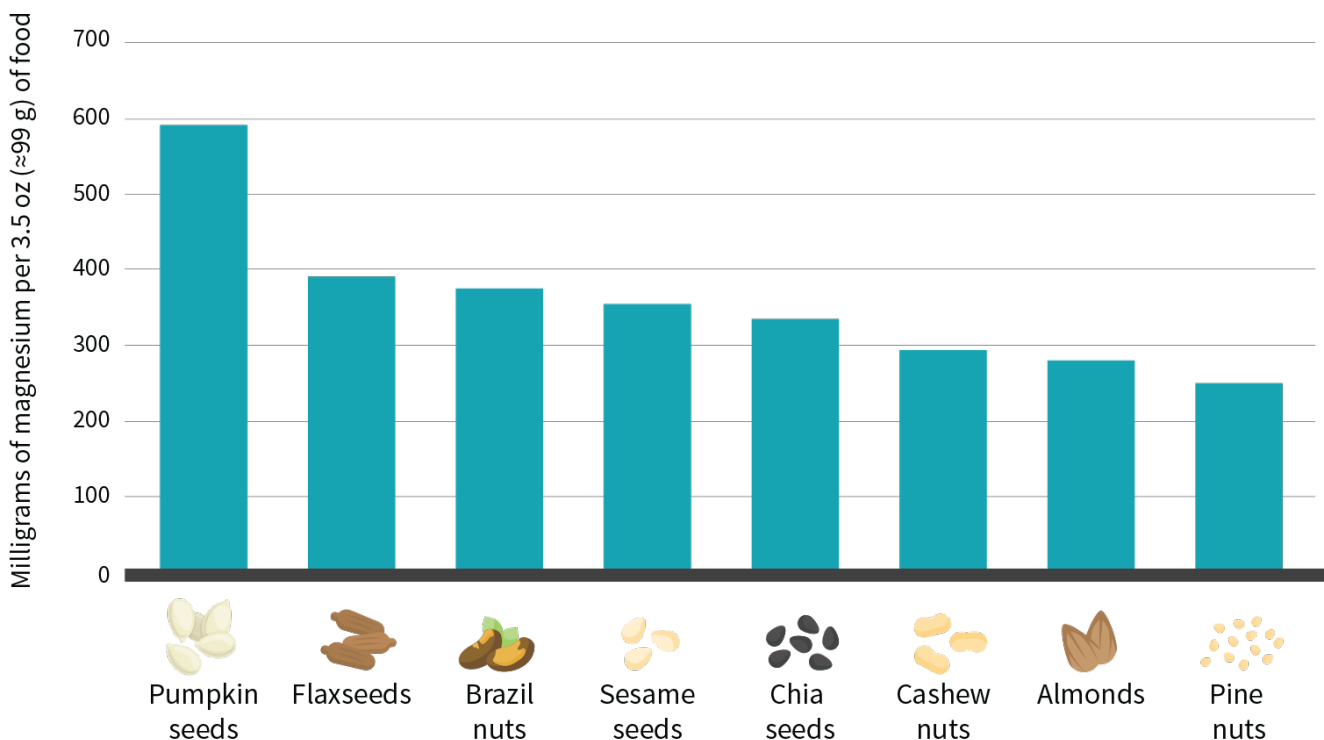
What makes *magnesium* a secondary option

Like [calcium](#), magnesium is one of the major mineral components of bone.^[128] Low levels in the blood are associated with bone loss; conversely, high levels are associated with greater bone mass in old age.

[Hypomagnesemia](#) (suboptimal magnesium levels in the blood) has been linked to neuromuscular and cardiovascular disorders,^[129] inflammatory diseases,^[130] and neurological disorders^{[131][132]} such as [Alzheimer's disease](#) (actually, suboptimal levels in the blood aren't associated with Alzheimer's; but suboptimal levels in the hair and the cerebrospinal fluid are^[133]). Hypomagnesemia can also result in abnormal nervous-system stimulation leading to [anxiety](#) and [poor sleep](#). In older people with hypomagnesemia, supplemental magnesium has been shown to [improve sleep quality](#).^{[134][135]}

In people with low magnesium intakes, magnesium supplementation has been shown to raise slightly both [total testosterone and the percentage of free testosterone](#) (the percentage your body can use most easily).^[136]

Magnesium content of seeds and nuts (mg)



Reference: USDA Food Composition Databases. Accessed September 27, 2019. <https://ndb.nal.usda.gov/ndb/>

Who is more likely to have low magnesium levels?

- *Older people*, because they tend to have relatively low magnesium intakes^[137] and may absorb less during digestion.^[138]
- *People who sweat a lot*, because magnesium is lost through sweat. Athletes participating in sports requiring weight control may be especially vulnerable.

- *Type 2 diabetics*. It has been estimated that, over all adult ages in developed countries, hypomagnesemia affects less than 15% of healthy people but up to 50% of people with type 2 [diabetes](#).^[139]

In addition, certain [diuretics](#), [proton pump inhibitors](#), and the antifungal medicine [amphotericin-b](#) can cause significant magnesium loss.^[140] [amiloride](#)] (<https://www.fda.gov/Drugs/DrugSafety/ucm245011https://ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/> However, potassium-sparing diuretics (e.g., [<https://medlineplus.gov/druginfo/meds/a615029.html>]), [eplerenone](#)/Inspra, [spironolactone](#)/Aldactone, [triamterene](#)/Dyrenium) may not.^[140]

Warnings about *magnesium*

High doses of supplemental magnesium can cause diarrhea and general intestinal discomfort.^[141] Fortunately, magnesium obtained via food has not been seen to cause such problems.^[141]

Tolerable Upper Intake Level (UL) for supplemental magnesium (mg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–12 months	—	—	—	—
1–3 years	65	65	—	—
4–8 years	110	110	—	—
>8 years	350	350	350	350

Reference: Institute of Medicine. [Magnesium](#) (chapter 6 in *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. The National Academies Press. 1997. DOI:[10.17226/5776](https://doi.org/10.17226/5776)).

Magnesium can lower blood sugar and may have additive effects when taken with other supplements or pharmaceuticals that can lower blood sugar, such as [diabetes medicines](#).

Magnesium may impair the absorption of some pharmaceuticals, notably [bisphosphonates](#) and [antibiotics](#) — especially antibiotics in the [tetracycline class](#) (e.g., doxycycline) and [quinolone class](#) (e.g., ciprofloxacin).^[142] Take magnesium at least 6 hours before or after taking bisphosphonates or antibiotics.

Since [calcium](#), [iron](#), magnesium, and [zinc](#) compete for absorption, it is better to take them at least one hour apart.

Because magnesium might have a sedative effect, it is often supplemented before bed.

How to take *magnesium*

There is no single, agreed-upon, satisfactory method for assessing magnesium status^[143] (as we saw, suboptimal levels in the blood aren't associated with Alzheimer's, but suboptimal levels in the hair and the cerebrospinal fluid are^[133]).

We said that older people tend to have relatively low magnesium intakes, but to get a better sense of *your* typical magnesium intake, you should track what you eat for a week. If, on average, you are getting less than 80% of your Recommended Dietary Allowance (RDA), supplementation becomes an option, though first you should try to eat more [foods rich in magnesium](#).

Recommended Dietary Allowance (RDA) for magnesium (mg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	30*	30*	—	—
7–12 months	75*	75*	—	—
1–3 years	80	80	—	—
4–8 years	130	130	—	—
9–13 years	240	240	—	—
14–18 years	410	360	400	360
19–30 years	400	310	350	310
31–50 years	420	320	360	320
>50 years	420	320	—	—

* Adequate intake (AI)

Reference: Institute of Medicine. [Magnesium](#) (chapter 6 of *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. The National Academies Press. 1997. DOI:[10.17226/5776](#))

If, for some reason, you cannot get enough magnesium through foods, start supplementing with *200 mg* once a day. Capsules with 400 mg are common, but keep in mind that the Tolerable Upper Intake Level (UL) for supplemental magnesium is 350 mg. The higher the dose, the higher the risk of gastrointestinal issues.

Commonly supplemented [forms](#) include citrate, gluconate, and glycinate. To increase absorption, magnesium gluconate should be taken with food; other forms can also be taken on an empty stomach. *Avoid magnesium oxide*: it has poor bioavailability (rats absorbed only 15% in one study,^[144] humans only 4% in another^[145]) and is especially liable to cause intestinal discomfort and diarrhea.^{[145][146][147]}

Because magnesium might improve sleep quality, it is often supplemented before bed.

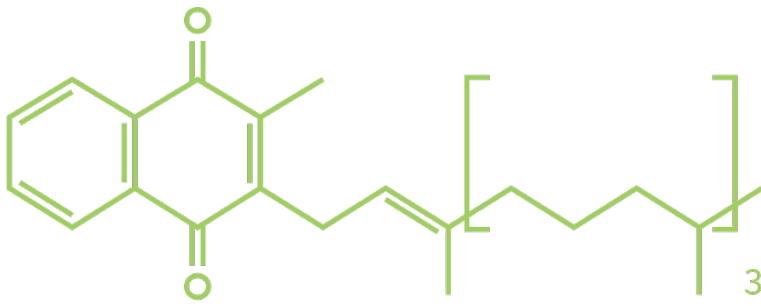
Vitamin K

What makes *vitamin K* a secondary option

Vitamin K is an umbrella term for a variety of molecules with similar but distinct structures.

- K₁ ([phyloquinone](#)) is a molecule found in plants.
- K₂ ([menaquinone](#)) is a group of molecules.
 - K₂ MK-4 is mostly found in animal products.
 - K₂ MK-7 is mostly found in fermented foods.

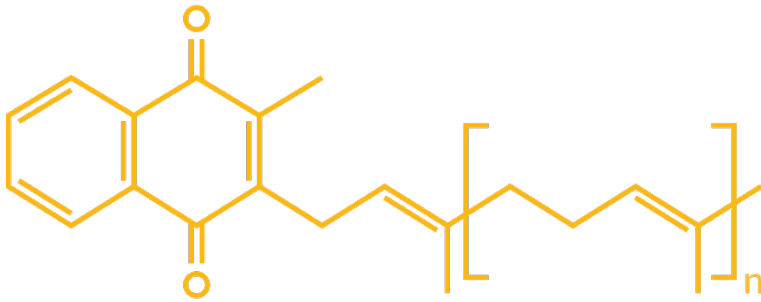
The K vitamins



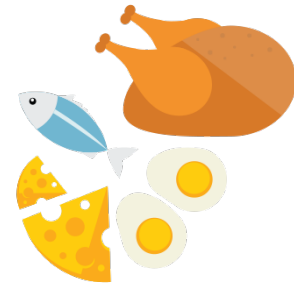
Phylloquinone (Vitamin K₁)



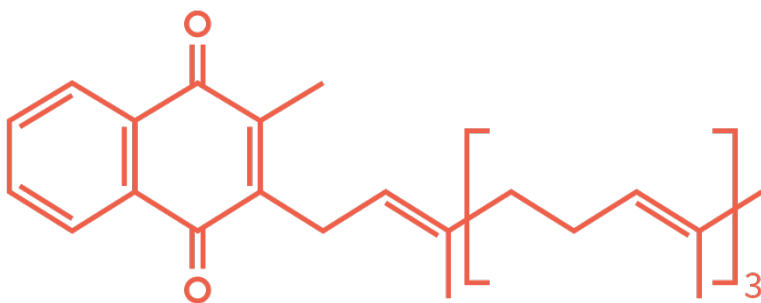
Found in plants



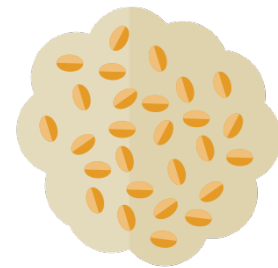
Menaquinone-4 (Vitamin K₂ MK-4)



Found in animal products



Menaquinone-7 (Vitamin K₂ MK-7)



Found in fermented foods

The accumulation of calcium in body tissues, notably bone, is called calcification. For bones, calcification is a good thing, but it can harden soft tissues, such as blood vessels — including coronary arteries, which supply oxygenated blood to the heart.

In all its forms, vitamin K is fat-soluble and supports blood clotting and [calcium](#) regulation; it helps ensure that more calcium gets deposited in bone and less in soft tissues. Hence, vitamin K can both strengthen the bones of older people (with more evidence in postmenopausal females) and reduce cardiovascular risk. However, there are notable differences between the different forms.

After being absorbed by your intestines, K₁ is taken up by your liver (where vitamin K is used to make clotting proteins, which are then released into your blood) at a higher rate than MK-4, whereas MK-4 is taken up by soft tissues at a higher rate than K₁. This should make K₁ better at supporting coagulation (i.e., blood clotting), and MK-4 better at preventing calcium from being deposited in the arteries.

Some K₁ converts indirectly to MK-4, but how much is unknown. Diets naturally rich in K₁ do not seem to reduce cardiovascular risk, but trials supplementing high K₁ doses have noted some reduction in coronary artery calcification. The reason may be that, in many plants, K₁ is tightly bound to chloroplasts (organelles

that contain chlorophyll and conduct photosynthesis), so you could be absorbing very little of what you eat.

Unlike MK-4, MK-7 has been used in trials looking at arterial stiffness and atherosclerosis, and we can say it is likely good at both supporting coagulation and preventing coronary calcification. It is important to note that cardiovascular research has not compared K₁ to K₂, or MK-4 to MK-7.

When it comes to bones, a few MK-4 trials looked at fracture risk and reported a decrease. One K₁ trial looked at fracture risk and reported a decrease, but without a concomitant increase in bone mineral density, so more research is needed to clarify the issue. Some MK-7 trials found an improvement in bone mineral density, but none have looked at fracture risk.

The vitamins K and D increase separately and synergistically the rate at which minerals (notably calcium and magnesium) accumulate in bones. MK-4 and MK-7 appear to do so more reliably than K₁.

Micrograms of vitamin K per 100 grams of food

FOODS	K~1~	K~2~ MK-4	K~2~ MK-7
Collards	440	0	0
Spinach	360–380	0	0
Broccoli	113–180	0	0
Cabbage	98–145	0	0
Natto	Not measured	0	939–998
Chicken	0–4.5	8.5–60	0
Pork	0–3.4	2.1–6	0.5–0.12
Beef	0.7–2.4	1.1–15	0–0.12
Beef liver	2.7	0.82	18.2
Egg	0.3–12	7–9	Not measured
Egg yolk	Not measured	15.5–64	0
Butter	7	15–21	0
Blue cheese	Not measured	Not measured	2.5–22
Cheddar	2.1	10.2	0–2.3

References: Fu et al. *J Agric Food Chem.* 2016.^[148] ● Manoury et al. *J Dairy Sci.* 2013.^[149] ● Booth. *Food Nutr Res.* 2012.^[150] ● Kamao et al. *J Nutr Sci Vitaminol (Tokyo).* 2007.^[151] ● Elder et al. *J Agric Food Chem.* 2006.^[152] ● Schurgers and Vermeer. *Haemostasis.* 2000: PMID:11356998^[153] ● Booth et al. *J Am Diet Assoc.* 1996.^[154] ● Shimogawara and Muto. *Arch Biochem Biophys.* 1992.^[155] ● Hirauchi et al. *J Chromatogr.* 1989.^[156]

Warnings about *vitamin K*

Vitamin K is usually safe. Supplementation might cause some nausea or stomach upset, but those effects are uncommon.

K₁ is present mostly in leafy green vegetables, many of which are cruciferous. If you plan to increase your K₁ intake through plant foods, be aware that cruciferous vegetables contain goitrogens and thus can reduce

thyroid hormone production. If you tend to eat a lot of cruciferous vegetables, such as kale, make sure to also get enough [iodine](#) — through iodine-rich foods (such as cod, shrimp, milk, yogurt, or cottage cheese), iodine-fortified foods (such as iodized salt), or supplements (75–150 mcg/day).

[K₁](#) and [K₂](#) are the only natural forms of vitamin K, but there exist several synthetic forms, the best known of which is [K₃](#) ([menadione](#)). However, whereas the natural forms of vitamin K are safe, even in high doses, [K₃](#) interfere with [glutathione](#), your body’s main antioxidant. [K₃](#) was once used to treat vitamin K deficiency in infants, but it caused liver toxicity, jaundice, and hemolytic anemia. Nowadays, it is used only in animal feed, in small doses. In animals, vitamin [K₃](#) gets converted into [K₂](#) MK-4, which you can consume safely.^[157]

Do not supplement with vitamin K if you have been prescribed blood thinners (i.e., [anticoagulants](#)) that work by hindering vitamin K’s blood-clotting properties, such as [warfarin](#) (Coumadin) or [acenocoumarol](#) (Sintrom). If you have been prescribed a diet low in vitamin K, you may need to strictly track your vitamin K intake to ensure it stays consistent.

[Orlistat](#) (Alli, Xenical) reduces how much fat you absorb from the food you eat. As a result, it also reduces the absorption of fat-soluble vitamins. If you take this medicine, take your vitamin K supplement at least 2 hours before or after.

How to take *vitamin K*

As we saw, different forms of vitamin K have different metabolisms and distributions within the body, so taking more than one form may be beneficial.

For *bone health*, take 200 mcg (0.2 mg) of *MK-7* and/or 45,000 mcg (45 mg) of *MK-4*. *MK-4* is the form best supported by the evidence, but more studies are needed to determine if smaller doses are also beneficial.

For *cardiovascular health*, take 200 mcg (0.2 mg) of *MK-7* and, optionally, 500–1,000 mcg (0.5–1 mg) of *K₁*.

Vitamin K being fat soluble, it is better absorbed when taken with a fat-containing food or supplement (e.g., [fish oil](#)).

The doses above reflect the doses used in studies; they are much higher than the minimum amount of vitamin K you need to avoid deficiency-related issues:

Adequate Intake (AI) for vitamin K (mcg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	2.0	2.0	—	—
7–12 months	2.5	2.5	—	—
1–3 years	30	30	—	—
4–8 years	55	55	—	—
9–13 years	60	60	—	—
14–18 years	75	75	75	75

AGE	MALE	FEMALE	PREGNANT	LACTATING
>18 years	120	90	90	90

Reference: Institute of Medicine. [Vitamin K](#) (chapter 5 in *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. The National Academies Press. 2001. DOI:[10.17226/10026](#))

Promising Supplements

Cholinergics

What makes *cholinergics* a promising option

A supplement is said to be cholinergic when it increases the brain's levels of acetylcholine, a major neurotransmitter associated with [memory](#) and [attention](#) span. Cholinergics may improve [cognition](#) in people experiencing [cognitive decline](#), and very preliminary evidence indicates they might benefit people with dementia.^[158]

[CDP-choline](#) (citicoline) can provide the brain with the choline it needs to produce more acetylcholine ([choline bitartrate](#) is much cheaper, but little of it seems to reach the brain^[159]). CDP-choline is also a source of [uridine](#), which has itself been hypothesized to improve cognition (though much more research is needed before it can be recommended for supplementation on its own). In addition, CDP-choline might improve vision in people suffering from glaucoma.

Warnings about *cholinergics*

Some temporary side effects, such as nausea and heartburn, have been documented in people taking CDP-choline. The interactions between CDP-choline and other supplements and pharmaceuticals are not well known.

The cholinergic [Huperzine-A](#) can inhibit acetylcholinesterase, an enzyme that breaks down the neurotransmitter acetylcholine; as a result, the brain's levels of acetylcholine increase. Its half-life exceeds 24 hours (i.e., after 24 hours, more than half of the dose you took will still be in your system), so it accumulates in the body when taken daily, which is problematic since long-term studies are scarce. There is a possibility that, over time, the body could adapt by producing more acetylcholinesterase, which would lead to reduced acetylcholine levels and a withdrawal period after huperzine-A supplementation has ceased. While the doses used in the studies (0.2–0.99 mg) were deemed safe in the short term, long-term supplementation cannot be recommended.

How to take *cholinergics*

To supplement with *CDP-choline* for cognitive improvements, take 500–2,000 mg/day.

To supplement with *CDP-choline* against glaucoma, take 1,600 mg/day.^[160]

Maca (for symptoms of menopause))

What makes *Maca* a promising option

The [symptoms of menopause](#) are vast and often troublesome, and there's probably no single thing that can help with all or even most of them. In the case of Maca, several studies have been conducted and, overall, they mostly suggest a small but potentially meaningful improvement in general symptoms.^{[124][161][162][163][164][165]}

Which symptoms they reduce are fairly inconsistent, with some studies suggesting a reduction in [depression](#), [headaches](#), and hot flashes, while some didn't suggest effects. Decreases in [anxiety](#) and nervousness and improvements in [sleep quality](#) are the most consistent benefits.

Warnings about *maca*

Maca is not known to interact with any major hormones (such as [DHEA](#), [estrogen](#), or [testosterone](#)) or any pharmaceuticals. To date, however, research into maca's potential adverse effects is somewhat limited.

How to take *maca*

Take 2–3.5 g of maca root powder at breakfast.

Vitamin E

What makes *vitamin E* a promising option

As you age, your immune system weakens against invaders and stressors. Supplementation with vitamin E can improve markers of immune function, but this does not necessarily translate into a reduced risk of catching infectious diseases. The evidence in this area is very mixed.^{[166][167]}

Still, although more research is needed to better understand the effects of vitamin E on infection rates and illness severity, current evidence suggests that seniors can benefit from vitamin E supplementation.

Warnings about *vitamin E*

Vitamin E has both antiplatelet and anticoagulant properties — the latter because it interferes with the blood-clotting properties of [vitamin K](#).^[168] This could be a problem for people whose diet is poor in vitamin K or who take blood thinners, be they antiplatelet agents (such as [aspirin](#)) or anticoagulants (such as [warfarin](#)/Coumadin and [acenocoumarol](#)/Sintrom).

Moreover, because of these antiplatelet and anticoagulant properties, 200 IU of vitamin E (the dose recommended for daily supplementation) may lower systolic [blood pressure](#).^[169] Note that supplements and pharmaceuticals that lower blood pressure can have cumulative effects.

[Orlistat](#) (Alli, Xenical) reduces how much fat you absorb from the food you eat. As a result, it also reduces the absorption of fat-soluble vitamins. If you take this medicine, take your vitamin E supplement at least 2 hours before or after.

How to take *vitamin E*

Track what you eat for a week; if, on average, you are getting less than 80% of your Recommended Dietary Allowance, supplementation becomes an option, though first you should try eating more [foods rich in vitamin E](#).

Alternatively, you could [check your blood levels](#) of vitamin E. Blood levels of alpha-tocopherol (α -tocopherol) under 0.5 mg/dL (<5 mcg/mL, or <11.5 μ mol/L) are considered deficient.

Recommended Dietary Allowance (RDA) for vitamin E (alpha-tocopherol) (mg / IU)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	4 / 6*	4 / 6*	—	—
7–12 months	5 / 7.5*	5 / 7.5*	—	—
1–3 years	6 / 9	6 / 9	—	—
4–8 years	7 / 10.4	7 / 10.4	—	—
9–13 years	11 / 16.4	11 / 16.4	—	—
>13 years	15 / 22.4	15 / 22.4	15 / 22.4	19 / 28.4

* Adequate Intake (AI)

Reference: Institute of Medicine. [Vitamin E](#) (chapter 6 in *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. The National Academies Press. 2000.)^[170]

Take 200 IU of vitamin E (134 mg of natural α -tocopherol or 90 mg of synthetic α -tocopherol^[170]). Do not take more than 400 IU/day, and since vitamin E has anticoagulant properties, make sure your diet contains at least your [Adequate Intake \(AI\) of vitamin K](#) (90 mcg/day for females; 120 mcg/day for males).

Vitamin E being fat soluble, it is better absorbed when taken with a fat-containing food or supplement (e.g., [fish oil](#)).

Unproven Supplements

Vinegar

What makes *vinegar* an unproven supplement

Acetic acid is, after water, the main component of vinegar. It may slow the passage of food from the stomach to the small intestines, thus slowing the [absorption of carbohydrates](#), thus reducing both [insulin](#) response and damage from hyperglycemia. It may also improve insulin signaling via various molecular mechanisms.^[171]

The overall research suggests a smaller increase in post-meal [blood glucose](#) when vinegar is taken before or with a meal,^[172] but this reduction is modest and doesn't last long (roughly 2 hours). Moreover, the studies are small and short-term, and their methodologies don't give us full confidence in their findings.

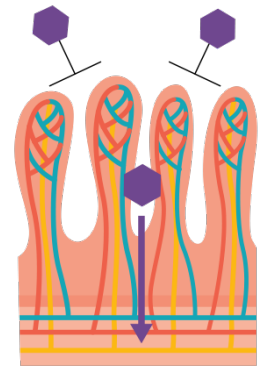
As for the reductions in [HbA1c](#) (a biomarker of glucose metabolism) and fasting blood glucose, they may not be strong enough to have a meaningful, long-term effect on health, and they're supported by scant evidence in the first place.^{[173][174][175][176][177][178]}

Vinegar's proposed mechanism of action

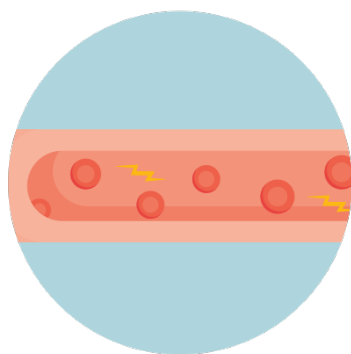
... slow gastric emptying



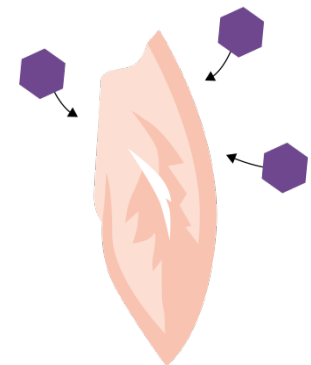
... inhibit intestinal carb absorption



Acetic acid may ...



... increase blood flow



... increase cellular glucose uptake

In short, vinegar's ability to prevent or treat type 2 diabetes is uncertain, as is its long-term benefit for people with impaired glucose tolerance. You should wait for studies of higher quality, including long-term studies, before you go out of your way to take vinegar with all your meals.

However, if you want to give vinegar a try anyway, here is the dose best supported by current evidence:

- 2.8 g/day of acetic acid divided into 1.4 g doses taken right before breakfast and dinner

Alternatively, you can take the following.

- 2 tablespoons (29.6 mL) of apple cider vinegar right before breakfast and dinner (59.2 mL/day; which is approximately 3.6 grams of acetic acid per day)

Vitamin B₇ (biotin)

What makes *biotin* an unproven supplement

Caution: Biotin can affect laboratory results

Biotin can interfere with many laboratory tests, from [hormone tests](#) to [cardiovascular diagnostics](#). Cease supplement 3 to 7 days before getting any lab work done.

Biotin, also known as vitamin B₇, partakes in the production of keratin, the protein at the core of hair and nails. For that reason, it is highly popular as a supplement to improve the [appearance](#) of hair and nails.^{[179][180]}

As it stands, no *randomized control trials* (RCTs) have tested biotin's effects on the hair or nails of healthy people,^[181] but supplementation may promote healthy hair and nails in people with the following conditions:

- [Biotin deficiency](#) (which is rare, though maybe less so in people experiencing hair loss)^{[181][182]}
- Genetic disorders affecting biotin metabolism (leading to a deficiency in two enzymes responsible for processing biotin: [biotinidase](#) and [holocarboxylase synthetase](#))^{[181][183]}
- Some nail medical conditions ([brittle nails](#), triangular worn-down nails, trachyonychia, and habit-tic deformity)^{[184][185][186][187][188][189]}
- [Uncombable hair syndrome](#)^{[179][190][191]}
- Medication-induced hair loss (caused by [valproic acid](#), for example)^{[192][193][194]}

The studies on biotin supplementation for the above conditions are mostly case studies that provide preliminary, if encouraging, data. People who are biotin deficient or have inborn errors of biotin metabolism are the most likely to benefit from supplementation.

In cases of *genetic disorder affecting biotin metabolism*, larger biotin doses (10–30 mg/day) have helped.^[181]

In cases of *biotin deficiency* or *medical condition* (brittle nails, uncombable hair syndrome, etc.), 0.3–3 mg/day may be beneficial.^[181]

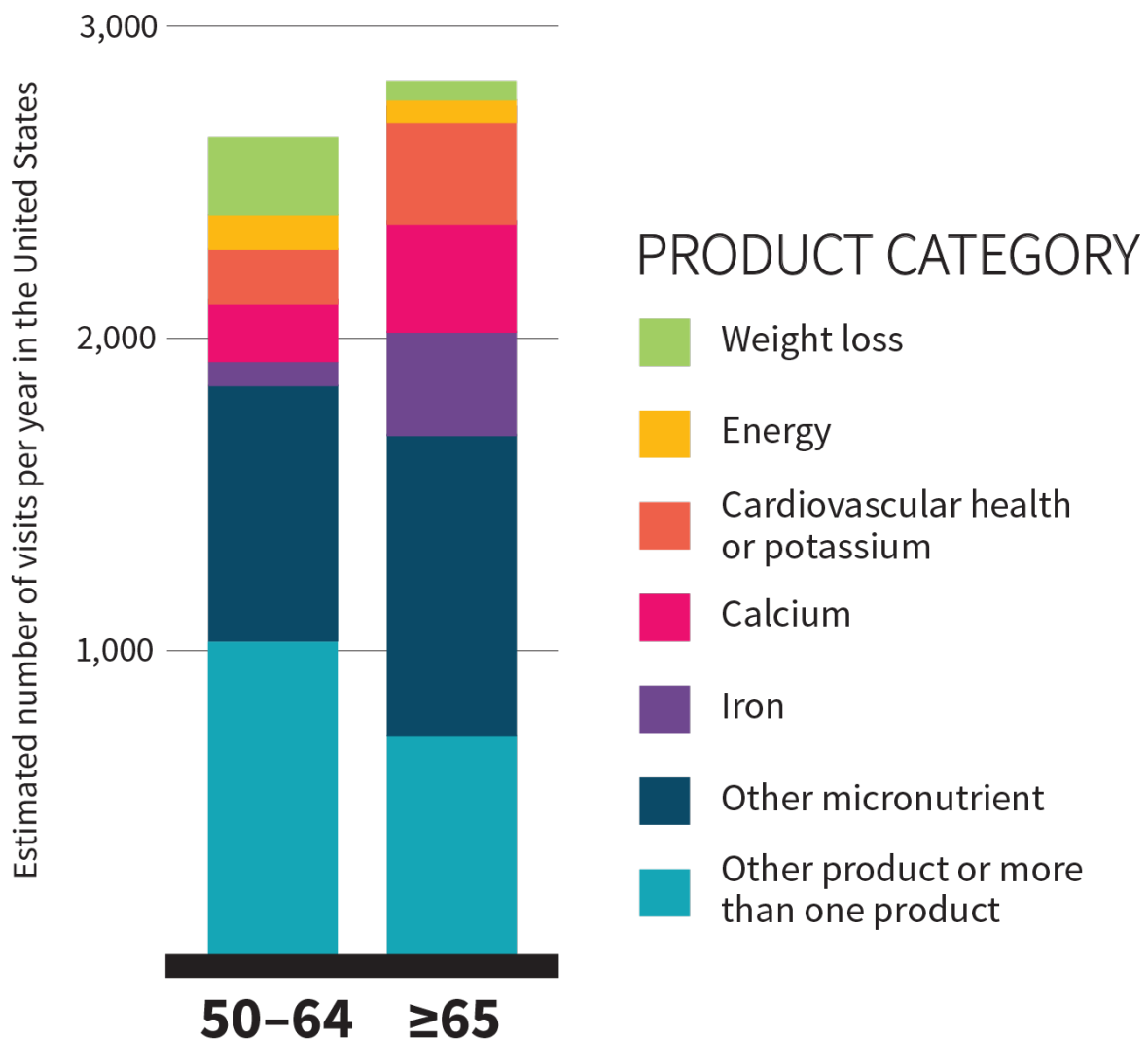
Inadvisable Supplements

Iron

What makes *iron* an inadvisable supplement

Data gathered between 2004 and 2013 show that, in the United States, three micronutrients are responsible for almost a third of all supplement-related emergency-room visits of adults aged 65 or older: [calcium](#), [potassium](#), and iron.^[195] The study specifies that “swallowing problems caused most emergency department visits involving calcium products ..., whereas abdominal symptoms (e.g., nausea, vomiting, and abdominal pain) were frequently associated with iron or potassium products”.^[195]

Supplement-related emergency-room visits in people aged 50+



Adapted from Geller et al. *N Eng J Med.* 2015.^[195]

More iron isn't always better or even harmless. When too much iron builds up in your body ([hemochromatosis](#)), it becomes toxic and can lead to dysfunction in your heart, liver, and pancreas. In extreme cases, it can cause [arrhythmia](#), heart failure, and death.

Postmenopausal females need less iron (8 mg/day, like males) than premenopausal females (18 mg/day). Although iron deficiency contributes substantially to the high prevalence of [anemia](#) seen in the elderly,^{[196][197]} taking an iron supplement “just in case” (or because you look pale and feel tired) is ill-advised. If you think you might suffer from iron deficiency, see a physician and get tested.

Potassium

What makes *potassium* an inadvisable supplement

As mentioned above in the [iron](#) entry, potassium is one of the three micronutrients responsible for almost a third of all supplement-related emergency-room visits of adults aged 65 or more,^[195] mostly due to abdominal symptoms (e.g., nausea, vomiting, and abdominal pain).

Worse, too much potassium at once on an empty stomach can lead to [hyperkalemia](#) (very high levels of potassium in the blood) and thus to dangerous changes in heart rhythm ([arrhythmia](#)). For that reason, in the United States, supplemental potassium chloride (the most common form of supplemental potassium) in “solid oral” form (i.e., in tablets and capsules) is [limited to 99 mg](#) of [elemental potassium](#) per serving.





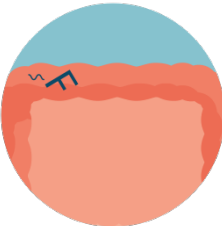
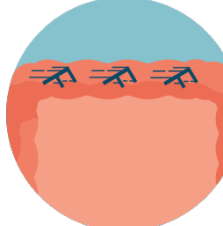
This is a very low amount, which makes it probable that the seniors who suffered from abdominal symptoms from potassium took more than one serving (or used a powder supplement, or took too much Nu-Salt®). It isn't a risk you want to take. If you suspect you might have low potassium levels, see a physician and get tested.

Vitamin B₉ (folate / folic acid)

What makes *vitamin B₉* an inadvisable supplement

Vitamin B₉ comprises folate and its synthetic form, folic acid. The Recommended Dietary Allowance (RDA) for vitamin B₉ is 400 mcg/day for males and most females; 600 mcg/day for pregnant females; and 500 mcg/day for lactating females. High doses of folic acid have been successfully used by pregnant females to prevent birth tube defects,^[73] which is why some foods, especially bread, are fortified with it.

Folate vs. folic acid

Folate	Folic acid
 <p data-bbox="411 349 719 432">Naturally occurring form of the vitamin</p>	 <p data-bbox="1150 342 1385 421">Synthetic form of the vitamin</p>
 <p data-bbox="411 622 743 752">Good sources of folate include chickpeas and lentils</p>	 <p data-bbox="1150 640 1374 719">Used to fortify many foods</p>
 <p data-bbox="400 954 730 1037">Mediocre absorption by the body</p>	 <p data-bbox="1150 947 1417 1030">Good absorption by the body</p>

Unfortunately, preliminary research suggests that high doses of folic acid (>1,000 mcg/day) may increase the risk of colon cancer in seniors and may exacerbate pre-existing colon cancer. Neither folic acid supplements nor [multivitamins](#), which most often contain too much folic acid, are recommended for seniors.

FAQ

Q. What about the supplements not covered in this guide?

Our guides are regularly updated, often with new supplements. We prioritize assessing (and reassessing) the most popular of them and those most likely to work. However, if there is a specific supplement you'd like to see covered in a future update, please let us know by [filling out this survey](#).

Q. Can I add a supplement not covered in this guide to my combo?

Supplement with your current combo for a few weeks before attempting any change. Talk to your physician and [research each potential addition](#). Check for known negative interactions with other supplements and pharmaceuticals in your current combo, but also for synergies. If two supplements are synergistic or additive in their effects, you might want to use lower doses of each.

Q. Can I modify the recommended doses?

If a supplement has a recommended dose range, stay within that range. If a supplement has a precise recommended dose, stay within 10% of that dose. Taking more than recommended could be counterproductive or even dangerous. Taking less could render the supplement ineffective, yet starting with half the regular dose could be prudent — especially if you know you tend to react strongly to supplements or pharmaceuticals.

Q. At what time should I take my supplements?

The answer is provided in the “How to take” section of a supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Starting with half the regular dose can help minimize the harm a supplement may cause when taken during the day (e.g., [fatigue](#)) or in the evening (e.g., [insomnia](#)).

Q. Should I take my supplements with or without food?

The answer is provided in the “How to take” section of a supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Besides, a supplement's digestion, absorption, and metabolism can be affected differently by different foods. Fat-soluble vitamins ([A](#), [D](#), [E](#), [K](#)), for instance, are better absorbed with a small meal containing fat than with a large meal containing little to no fat.

Q. What are DRI, RDA, AI, and UL?

The [Dietary Reference Intakes](#) (DRIs) is a system of nutrition recommendations designed by the Institute of Medicine (a US institution now known as the [Health and Medicine Division](#)). RDA, AI, and UL are part of this system.

- Contrary to what the name suggests, a *Recommended Dietary Allowance* (RDA) doesn't represent an *ideal* amount; it represents the *minimum* you need in order to avoid deficiency-related health issues. More precisely, it represents an amount just large enough to meet the minimum requirements of 97.5% of healthy males and females over all ages — which implies that the RDA is too low for 2.5% of healthy people.
- The *Adequate Intake* (AI) is like the RDA, except that the number is more uncertain.
- The *Tolerable Upper Intake Level* (UL) is the maximum safe amount. More precisely, it is the maximum daily amount deemed to be safe for 97.5% of healthy males and females over all ages — which implies that the UL is too high for 2.5% of healthy people.

As a general rule, a healthy diet should include at least the RDA of each nutrient — but less than this nutrient's UL. This rule has many exceptions, though. For instance, people who sweat more need more salt (i.e., sodium), whereas people who take [metformin](#) (a diabetes medicine) need more [vitamin B12](#).

Moreover, the DRIs are based on the median weight of [adults](#) and [children](#) in the United States. Everything else being equal (notably age, sex, and percentage of body fat), you likely need a lesser amount of nutrients if you weigh less, and vice versa if you weigh more. The numbers, however, are not proportional — if only because the brains of two people of very different weights have very similar needs. So you can't just double your RDIs for each nutrient if you weigh twice as much as the median adult of your age and sex (even if we overlook that people weighing the same can differ in many respects, notably body fat).

Q. What's the difference between elemental iron/magnesium/potassium and other kinds?

"Elemental" refers to the weight of the mineral by itself, separately from the compound bound to it. For instance, ingesting 500 mg of magnesium gluconate means ingesting 27 mg of elemental [magnesium](#).

Product labels display the elemental dosage. On a label, "27 mg of magnesium (as magnesium gluconate)" means 27 mg of elemental magnesium (and 473 mg of gluconic acid).

Q. Wait, where's calcium?

While [calcium](#) supplementation may promote bone health and reduce [blood pressure](#), it may also increase the risk of [hypercalcemia](#) (dangerously high levels of calcium in the blood), potentially leading to heart disease, the [leading cause of death](#) among older adults in the United States. The evidence on bone and heart health is mixed and still developing; whether or not the potential benefits outweigh the potential harm is still to be determined.

Q. What about multivitamins?

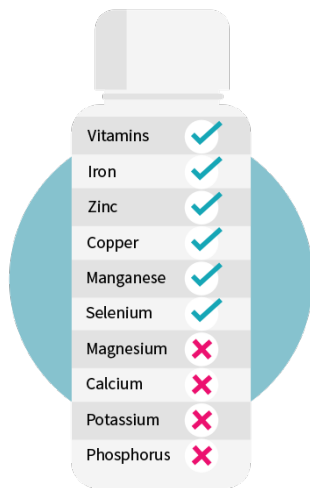
You may be inclined to take a [multivitamin](#) as a sort of insurance against nutritional deficiencies. A multivitamin isn't strictly necessary, but it can help *if it is well formulated*.

When buying a multivitamin, check on the label the content of each serving, the number of pills per serving, and the number of servings per day; don't pay more for dubious bells and whistles; and stick to a company with a reputation for good manufacturing.

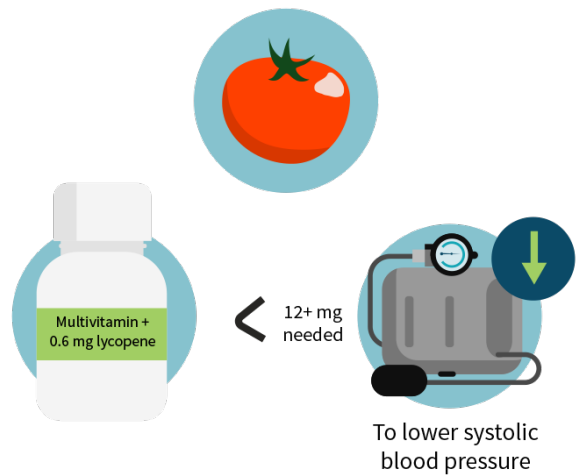
The form of the supplement can matter, too. [Magnesium](#) oxide, for instance, has very low bioavailability — not only will you absorb less [elemental magnesium](#) from it but it may also cause intestinal discomfort.

Factors to consider when buying a multivitamin

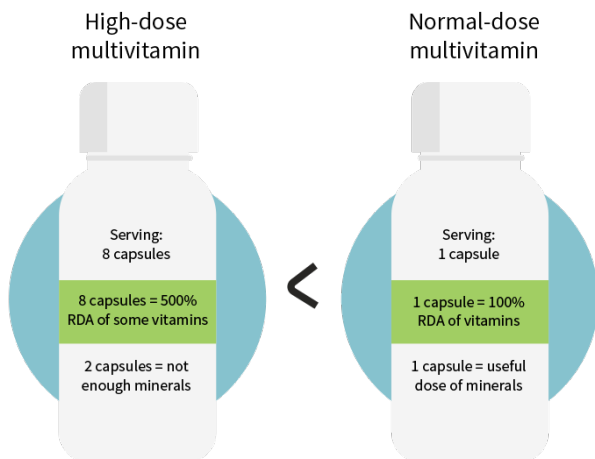
Multivitamins don't meet the RDAs for some micronutrients



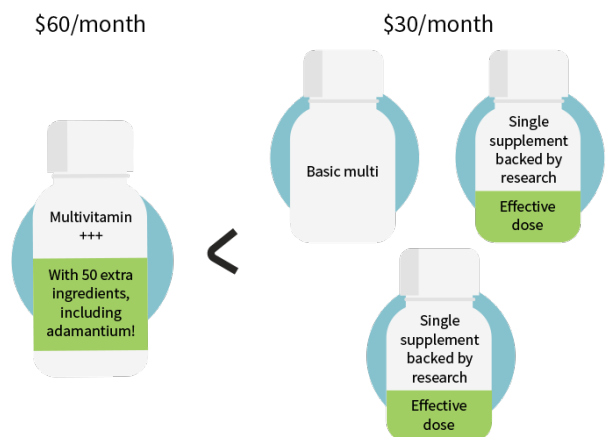
Multivitamins may contain extra ingredients but in too-small doses (e.g., lycopene)



High-dose multivitamins make you choose between too much of some vitamins and not enough minerals



Don't pay extra for multivitamins that contain many superfluous, often unproven ingredients



Always buy from a reputable company with good manufacturing practices.

Q. What's the difference between anthocyanins and anthocyanidins?

Anthocyanins contain anthocyanidins. To be more precise, an anthocyanidin is simply an anthocyanin without its sugar molecule(s).

Q. Can I replace blueberries with other anthocyanin-rich foods?

Most studies are on [blueberries](#), and the total amount of anthocyanins does not tell the whole story, because different *types* of anthocyanins can be found in different amounts in different berries. Studies on [cognition](#) have reported benefits from blue-purple anthocyanins, notably cyanidin and delphinidin, whereas red anthocyanins, such as pelargonidin, lack the same scientific backing.

So dark berries (blueberries, blackberries, elderberries ...) might be interchangeable for the purpose of enhancing cognition, whereas red berries (strawberries, raspberries ...), although also rich in anthocyanins, are likely not suitable alternatives.

Blue-purple anthocyanins can be found in foods other than dark berries, such as purple cauliflower, purple potatoes, and purple rice, but keep in mind that some blue-purple plants derive their color from betalains, not anthocyanins — for instance, beetroot.

Phytochemical profiles of select berries
(mg per 100 grams of edible portion)

FRUIT	TOTAL ANTHOCYANIDINS [*]	TOTAL FLAVAN-3-OLS ^{**}	TOTAL FLAVONOLS ^{**}
Chokeberry, raw	437.22	—	8.90
Bilberry	430.91	4.13	—
Black raspberry	324.02	—	—
Currant, black, raw	272.44	1.17	12.69
Blueberry	163.52	51.71	9.72
Blackberry	90.46	42.50	2.49
Red raspberry, raw	38.68	6.63	1.32
Strawberry	33.63	4.51	1.60
Cranberry, dried, sweetened	0.72	—	6.91
Cranberry juice cocktail	0.46	0.19	1.79
Cranberry sauce, canned, sweetened	0.14	—	5.11
Cranberry juice, unsweetened	—	0.92	20.82
Mulberry, raw	—	—	2.47

* Total anthocyanidins (cyanidin, delphinidin, peonidin, petunidin)

** Total flavan-3-ols ((-)-epicatechin, (-)-epicatechin-3-gallate, (-)-epigallocatechin, (-)-epigallocatechin-3-gallate, (+)-catechin,

(+)-galliccatechin)

*** Total flavonols (kaempferol, myricetin, quercetin)

Adapted from Basu et al. *Nutr Rev.* 2010.^[198]

Q. Are organic blueberries better?

In terms of anthocyanin content, not really: anthocyanin levels appear to be almost identical (within 5%) in organic and non-organic [blueberries](#) cultivated in the same area.^[33] On the other hand, there appear to be large differences depending on the soil. For example, even within the United States, the anthocyanin content can range from 144 to 823 mg per 100 grams of blueberries, depending on the region where the bushes are grown.^[33]

Q. Isn't soy protein *bad* for males?





Phytoestrogens are plant compounds structurally similar to estradiol, the main [estrogen](#) in males and premenopausal females. Because soy contains [isoflavones](#), a type of phytoestrogen, concern has been raised about soy affecting male health.

To this day, two case reports have documented adverse effects ([gynecomastia](#), [hypogonadism](#), reduced [libido](#), and [erectile dysfunction](#)) from an estimated 360 mg of soy isoflavones per day for 6–12 months. However, a meta-analysis of 15 *randomized controlled trials* (RCTs, a much higher level of evidence than case reports) found that males' levels of [total and free testosterone](#) were not notably affected by either 60–240 mg of isoflavones or 10–70 grams of soy protein per day.

Accordingly, a couple of scoops of soy protein powder are unlikely to have estrogenic effects in males. If you'd like to take more, however, look for a soy protein concentrate or isolate produced through the [alcohol-wash method](#), which dramatically lowers the isoflavone content.^[199]

Keep in mind that the isoflavone content of different soy products can vary depending on several factors, such as the variety of soybeans used, differences in growing and storage conditions, and differential food processing techniques employed.^[200] You can see how it varies below

Isoflavone content of common soy foods

Food category	Food	Milligrams of isoflavones per 100 g of food		
		Average	Minimum	Maximum
 Traditional unfermented soy foods	Edamame	18	14	19
	Soybeans (boiled)	65	23	128
	Soybeans (raw)	155	10	440
	Soybean sprouts	34	0	107
	Soy milk (unsweetened)	11	1	31
	Soy nuts	148	2	202
	Tofu	30	3	142
 Traditional fermented soy foods	Miso	41	3	100
	Miso soup	1.5	1.5	1.5
	Miso soup mix (powder)	70	54	126
	Natto	82	46	124
	Soy sauce	1	0	3
	Tempeh	61	7	179
 Second-generation soy foods	Soy-based veggie “meats”	9	0	23
	Soy cheeses	26	3	59
	Soy yogurt	33	10	70
 Soy flours and protein powders	Soy flour (defatted)	151	74	324
	Soy flour (full-fat)	165	130	260
	Soy infant formula (powder)	28	21	31
	Soy protein concentrate (alcohol wash)	12	2	32
	Soy protein concentrate (water wash)	95	61	167
	Soy protein isolate	91	46	200

Reference: USDA FoodData Central Databases. Accessed Jan 18, 2019. <https://fdc.nal.usda.gov/>

Q. Which dietary protein is best for bone health?

Most studies used dairy protein, yet the protein in our bones is mostly type 1 collagen. It follows that supplemental type 1 collagen should be optimal for bone health — and indeed, animal models appear to support this notion.

The few relevant human studies to date, however, had mixed results. Not only that, but they cumulated

factors (they gave collagen with [calcium](#), [vitamin D](#), dietary changes ...), making it impossible to determine which factor did what and to what extent. Until better human studies come along, collagen's superiority over other proteins (for bone health) will stay hypothetical.

Q. Don't dietary proteins *reduce* bone density?

More protein in the diet has been linked to more [calcium](#) in the urine. Two reasons have been suggested to explain this phenomenon:

- Your body draws from its calcium stores (in bones) to buffer the acid load caused by dietary protein. This has led researchers to suggest that higher protein intake could increase bone loss.^[201]
- Most studies that looked at protein intake and calcium excretion list dairy products as a protein source,^[202] so higher urinary calcium could simply be the result of higher calcium intake (i.e., more calcium in, more calcium out).

Therefore, looking only at calcium _excretion _wasn't enough. Subsequent studies showed that dietary protein promotes dietary-calcium absorption^[203] and that high protein intake "promotes bone growth and retards bone loss {whereas} low-protein diet is associated with higher risk of hip fractures."^[43] High-protein diets have also been shown to modestly suppress the decrease in [bone mineral density](#) caused by weight loss.^[204]

What happens is that when you ingest more protein, you absorb more of the calcium in your food, so less calcium ends up in your feces. Later, your body gets rid of the calcium it doesn't need, so more calcium ends up in your urine, but not as much as would have otherwise ended in your feces.^[44] Therefore, an increase in protein intake leads to an overall decrease in calcium excretion, which points to an increase in calcium retention. High-protein diets also raise your *insulin-like growth factor-1* (IGF-1),^[205] which promotes notably bone growth.^[206]

All in all, current evidence suggests that *protein's effect on bones is either neutral or beneficial*.^{[44][45]}

Q. I've heard that I should "load" creatine. What does that mean?

Loading creatine means taking a high daily dose for a few days before moving down to a smaller maintenance dose, which can be taken indefinitely. This is not necessary for effective supplementation, however; benefits may be felt sooner through loading, but they normalize after a few weeks.

If you wish to load creatine, take 20–25 g/day for 7 days (splitting your daily intake into smaller doses, taking them with some food, and drinking more fluids may help prevent intestinal discomfort). Take 5 g/day thereafter.

Q. Creatine doesn't seem to work for me. What should I do?

Some people are creatine nonresponders: the creatine they ingest largely fails to reach their muscles. Alternate forms of creatine, such as creatine ethyl-ester, have been marketed to nonresponders, but they lack scientific support. Currently, the best way to lessen creatine nonresponse is to take 5 grams twice a day, each time with protein and carbs, preferably close to a time of muscle contraction (i.e., before or after

your workout).

Note that even if supplemental creatine fails to enter your muscles it can still benefit you in other ways, such as by improving your body's methylation status (methylation being a way for your cells to help manage gene expression).

Q. Can testosterone boosters bring my testosterone back to normal?

[DHEA](#), [vitamin D](#), [magnesium](#), and [zinc](#) have been seen to raise low testosterone levels. Few other supplements seem to help at all.

A few trials back [Coleus forskohlii](#), but its numerous potential adverse effects make it a risky proposition, especially for older people.

You might also have heard of [D-aspartic acid](#), but its promising first trials were followed by several others that found that it didn't increase testosterone.

Some other supplements, such as [ginger](#) and [Eurycoma longifolia](#), might support testosterone levels only in infertile males (or in males with testicular damage).

Many other herbs, such as [horny goat weed](#), have not even been studied in humans yet.

Finally, keep in mind that a supplement can benefit your libido (as do [maca](#) and, according to a small number of studies, [Tribulus terrestris](#)), your mood, or your energy levels, yet not affect your testosterone.

References

1. Carlos López-Otín, Maria A Blasco, Linda Partridge, Manuel Serrano, Guido Kroemer [The hallmarks of aging](#). *Cell*. (2013 Jun 6)
2. Laura Dwyer-Lindgren, Amelia Bertozzi-Villa, Rebecca W Stubbs, Chloe Morozoff, Johan P Mackenbach, Frank J van Lenthe, Ali H Mokdad, Christopher J L Murray [Inequalities in Life Expectancy Among US Counties, 1980 to 2014: Temporal Trends and Key Drivers](#). *JAMA Intern Med*. (2017 Jul 1)
3. Benjamin Mayne, Oliver Berry, Campbell Davies, Jessica Farley, Simon Jarman [A genomic predictor of lifespan in vertebrates](#). *Sci Rep*. (2019 Dec 12)
4. Christopher J Lord, Alan Ashworth [The DNA damage response and cancer therapy](#). *Nature*. (2012 Jan 18)
5. Alexey A Moskalev, Mikhail V Shaposhnikov, Ekaterina N Plyusnina, Alex Zhavoronkov, Arie Budovsky, Hagai Yanai, Vadim E Fraifeld [The role of DNA damage and repair in aging through the prism of Koch-like criteria](#). *Ageing Res Rev*. (2013 Mar)
6. Franceschi C, Bonafè M, Valensin S, Olivieri F, De Luca M, Ottaviani E, De Benedictis G [Inflamm-aging. An evolutionary perspective on immunosenescence](#). *Ann N Y Acad Sci*. (2000 Jun)
7. K C Darr, E Schultz [Exercise-induced satellite cell activation in growing and mature skeletal muscle](#). *J Appl Physiol* (1985). (1987 Nov)
8. Behzad Bazgir, Rouhollah Fathi, Mojtaba Rezazadeh Valojerdi, Paul Mozdziaik, Alireza Asgari [Satellite Cells Contribution to Exercise Mediated Muscle Hypertrophy and Repair](#). *Cell J*. (Winter 2017)
9. Jennifer E Morgan, Peter S Zammit [Direct effects of the pathogenic mutation on satellite cell function in muscular dystrophy](#). *Exp Cell Res*. (2010 Nov 1)
10. Irina M Conboy, Thomas A Rando [Heterochronic parabiosis for the study of the effects of aging on stem cells and their niches](#). *Cell Cycle*. (2012 Jun 15)
11. Douglas R Green, Lorenzo Galluzzi, Guido Kroemer [Mitochondria and the autophagy-inflammation-cell death axis in organismal aging](#). *Science*. (2011 Aug 26)
12. D HARMAN [THE FREE RADICAL THEORY OF AGING: EFFECT OF AGE ON SERUM COPPER LEVELS](#). *J Gerontol*. (1965 Apr)
13. G C Kujoth, A Hiona, T D Pugh, S Someya, K Panzer, S E Wohlgemuth, T Hofer, A Y Seo, R Sullivan, W A Jobling, J D Morrow, H Van Remmen, J M Sedivy, T Yamasoba, M Tanokura, R Weindruch, C Leeuwenburgh, T A Prolla [Mitochondrial DNA mutations, oxidative stress, and apoptosis in mammalian aging](#). *Science*. (2005 Jul 15)
14. Caroline L Holley, Kate Schroder [The rOX-stars of inflammation: links between the inflammasome and mitochondrial meltdown](#). *Clin Transl Immunology*. (2020 Feb 10)
15. Adeel Safdar, Jacqueline M Bourgeois, Daniel I Ogborn, Jonathan P Little, Bart P Hettinga, Mahmood Akhtar, James E Thompson, Simon Melov, Nicholas J Mocellin, Gregory C Kujoth, Tomas A Prolla, Mark A Tarnopolsky [Endurance exercise rescues progeroid aging and induces systemic mitochondrial rejuvenation in mtDNA mutator mice](#). *Proc Natl Acad Sci U S A*. (2011 Mar 8)
16. Laura Castello, Marco Maina, Gabriella Testa, Gabriella Cavallini, Fiorella Biasi, Alessio Donati, Gabriella Leonarduzzi, Ettore Bergamini, Giuseppe Poli, Elena Chiarpotto [Alternate-day fasting reverses the age-associated hypertrophy phenotype in rat heart by influencing the ERK and PI3K signaling pathways](#). *Mech Ageing Dev*. (Jun-Jul 2011)
17. Sarah Pickles, Pierre Vigié, Richard J Youle [Mitophagy and Quality Control Mechanisms in Mitochondrial Maintenance](#). *Curr Biol*. (2018 Feb 19)
18. Christopher A Ross, Michelle A Poirier [Protein aggregation and neurodegenerative disease](#). *Nat Med*. (2004 Jul)
19. C Sóti, P Csermely [Molecular chaperones and the aging process](#). *Biogerontology*. (2000)
20. Ivan Dimauro, Neri Mercatelli, Daniela Caporossi [Exercise-induced ROS in heat shock proteins response](#). *Free Radic Biol Med*. (2016 Sep)
21. Cong Zhang, Ana Maria Cuervo [Restoration of chaperone-mediated autophagy in aging liver improves cellular maintenance and hepatic function](#). *Nat Med*. (2008 Sep)
22. Nuria Garatachea, Helios Pareja-Galeano, Fabian Sanchis-Gomar, Alejandro Santos-Lozano, Carmen Fiuza-Luces, María Morán, Enzo Emanuele, Michael J Joyner, Alejandro Lucia [Exercise attenuates the major hallmarks of aging](#). *Rejuvenation Res*. (2015 Feb)
23. Arnold YI Wong, Jaro Karppinen, Dino Samartzis [Low back pain in older adults: risk factors, management options and future directions](#). *Scoliosis Spinal Disord*. (2017 Apr 18)
24. Judith E Carroll, Steven W Cole, Teresa E Seeman, Elizabeth C Breen, Tuff Witarama, Jesusa M G Arevalo, Jeffrey Ma, Michael R Irwin [Partial sleep deprivation activates the DNA damage response \(DDR\) and the senescence-associated secretory phenotype \(SASP\) in aged adult humans](#). *Brain Behav Immun*. (2016 Jan)
25. Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, Hazen N, Herman J, Katz ES, Kheirandish-Gozal L, Neubauer DN, O'Donnell AE, Ohayon M, Peever J, Rawding R, Sachdeva RC, Setters B, Vitiello MV, Ware JC, Adams Hillard PJ [National Sleep Foundation's sleep time duration recommendations: methodology and results summary](#). *Sleep Health*. (2015 Mar)

26. Marie-Pierre St-Onge, Dymrna Gallagher [Body composition changes with aging: the cause or the result of alterations in metabolic rate and macronutrient oxidation?](#). *Nutrition*. (2010 Feb)
27. Hein S, Whyte AR, Wood E, Rodriguez-Mateos A, Williams CM [Systematic Review of the Effects of Blueberry on Cognitive Performance as We Age](#). *J Gerontol A Biol Sci Med Sci*. (2019 Jun 18)
28. Krikorian R, Shidler MD, Nash TA, Kalt W, Vinqvist-Tymchuk MR, Shukitt-Hale B, Joseph JA [Blueberry supplementation improves memory in older adults](#). *J Agric Food Chem*. (2010 Apr 14)
29. Boespflug EL, Eliassen JC, Dudley JA, Shidler MD, Kalt W, Summer SS, Stein AL, Stover AN, Krikorian R [Enhanced neural activation with blueberry supplementation in mild cognitive impairment](#). *Nutr Neurosci*. (2018 May)
30. Miller MG, Hamilton DA, Joseph JA, Shukitt-Hale B [Dietary blueberry improves cognition among older adults in a randomized, double-blind, placebo-controlled trial](#). *Eur J Nutr*. (2018 Apr)
31. Whyte AR, Cheng N, Fromentin E, Williams CM [A Randomized, Double-Blinded, Placebo-Controlled Study to Compare the Safety and Efficacy of Low Dose Enhanced Wild Blueberry Powder and Wild Blueberry Extract \(ThinkBlue™\) in Maintenance of Episodic and Working Memory in Older Adults](#). *Nutrients*. (2018 May 23)
32. Bowtell JL, Aboo-Bakkar Z, Conway ME, Adlam AR, Fulford J [Enhanced task-related brain activation and resting perfusion in healthy older adults after chronic blueberry supplementation](#). *Appl Physiol Nutr Metab*. (2017 Jul)
33. Stevenson D, Scalzo J [Anthocyanin composition and content of blueberries from around the world](#). *J Berry Res*. (2012 Sep)
34. Rodríguez-Bonilla P, López-Nicolás JM, Méndez-Cazorla L, García-Carmona F [Development of a reversed phase high performance liquid chromatography method based on the use of cyclodextrins as mobile phase additives to determine pterostilbene in blueberries](#). *J Chromatogr B Analyt Technol Biomed Life Sci*. (2011 May 1)
35. Rimando AM, Kalt W, Magee JB, Dewey J, Ballington JR [Resveratrol, pterostilbene, and piceatannol in vaccinium berries](#). *J Agric Food Chem*. (2004 Jul 28)
36. Rimando A, Barney D [Resveratrol and naturally occurring analogues in vaccinium species](#). *Acta Hort*. (2005)
37. Montgomery SA, Thal LJ, Amrein R [Meta-analysis of double blind randomized controlled clinical trials of acetyl-L-carnitine versus placebo in the treatment of mild cognitive impairment and mild Alzheimer's disease](#). *Int Clin Psychopharmacol*. (2003 Mar)
38. Smeland OB, Meisingset TW, Borges K, Sonnewald U [Chronic acetyl-L-carnitine alters brain energy metabolism and increases noradrenaline and serotonin content in healthy mice](#). *Neurochem Int*. (2012 Jul)
39. Asadi M, Rahimlou M, Shishehbor F, Mansoori A [The effect of l-carnitine supplementation on lipid profile and glycaemic control in adults with cardiovascular risk factors: A systematic review and meta-analysis of randomized controlled clinical trials](#). *Clin Nutr*. (2019 Feb 22)
40. Serban MC, Sahebkar A, Mikhailidis DP, Toth PP, Jones SR, Muntner P, Blaha MJ, Andrica F, Martin SS, Borza C, Lip GY, Ray KK, Rysz J, Hazen SL, Banach M [Impact of L-carnitine on plasma lipoprotein\(a\) concentrations: A systematic review and meta-analysis of randomized controlled trials](#). *Sci Rep*. (2016 Jan 12)
41. Shang R, Sun Z, Li H [Effective dosing of L-carnitine in the secondary prevention of cardiovascular disease: a systematic review and meta-analysis](#). *BMC Cardiovasc Disord*. (2014 Jul 21)
42. DiNicolantonio JJ, Lavie CJ, Fares H, Menezes AR, O'Keefe JH [L-carnitine in the secondary prevention of cardiovascular disease: systematic review and meta-analysis](#). *Mayo Clin Proc*. (2013 Jun)
43. Shams-White MM, Chung M, Du M, Fu Z, Insogna KL, Karlson MC, LeBoff MS, Shapses SA, Sackey J, Wallace TC, Weaver CM [Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation](#). *Am J Clin Nutr*. (2017 Jun)
44. Calvez J, Poupin N, Chesneau C, Lassale C, Tomé D [Protein intake, calcium balance and health consequences](#). *Eur J Clin Nutr*. (2012 Mar)
45. Fenton TR, Lyon AW, Eliasziw M, Tough SC, Hanley DA [Meta-analysis of the effect of the acid-ash hypothesis of osteoporosis on calcium balance](#). *J Bone Miner Res*. (2009 Nov)
46. Janssen I, Heymsfield SB, Ross R [Low relative skeletal muscle mass \(sarcopenia\) in older persons is associated with functional impairment and physical disability](#). *J Am Geriatr Soc*. (2002 May)
47. Burd NA, Gorissen SH, van Loon LJ [Anabolic resistance of muscle protein synthesis with aging](#). *Exerc Sport Sci Rev*. (2013 Jul)
48. Mcleod JC, Stokes T, Phillips SM [Resistance Exercise Training as a Primary Countermeasure to Age-Related Chronic Disease](#). *Front Physiol*. (2019 Jun 6)
49. Moore DR, Churchward-Venne TA, Witard O, Breen L, Burd NA, Tipton KD, Phillips SM [Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men](#). *J Gerontol A Biol Sci Med Sci*. (2015 Jan)
50. Bell SJ [Whey protein concentrates with and without immunoglobulins: a review](#). *J Med Food*. (2000 Spring)
51. von Herrath D, Saube J, Hirschberg R, Rottka H, Schaefer K [Glomerular filtration rate in response to an acute protein load](#). *Blood Purif*. (1988)
52. Brenner BM, Meyer TW, Hostetter TH [Dietary protein intake and the progressive nature of kidney disease: the role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, renal ablation, and intrinsic renal disease](#). *N Engl J Med*. (1982 Sep 9)

53. Devries MC, Sithamparapillai A, Brimble KS, Banfield L, Morton RW, Phillips SM [Changes in Kidney Function Do Not Differ between Healthy Adults Consuming Higher- Compared with Lower- or Normal-Protein Diets: A Systematic Review and Meta-Analysis.](#) *J Nutr.* (2018 Nov 1)
54. Poortmans JR, Dellalieux O [Do regular high protein diets have potential health risks on kidney function in athletes?.](#) *Int J Sport Nutr Exerc Metab.* (2000 Mar)
55. Trumbo P, Schlicker S, Yates AA, Poos M, Food and Nutrition Board of the Institute of Medicine, The National Academies [Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids.](#) *J Am Diet Assoc.* (2002 Nov)
56. Rafii M, Chapman K, Owens J, Elango R, Campbell WW, Ball RO, Pencharz PB, Courtney-Martin G [Dietary protein requirement of female adults >65 years determined by the indicator amino acid oxidation technique is higher than current recommendations.](#) *J Nutr.* (2015 Jan)
57. Rafii M, Chapman K, Elango R, Campbell WW, Ball RO, Pencharz PB, Courtney-Martin G [Dietary Protein Requirement of Men >65 Years Old Determined by the Indicator Amino Acid Oxidation Technique Is Higher than the Current Estimated Average Requirement.](#) *J Nutr.* (2016 Mar 9)
58. Tang M, McCabe GP, Elango R, Pencharz PB, Ball RO, Campbell WW [Assessment of protein requirement in octogenarian women with use of the indicator amino acid oxidation technique.](#) *Am J Clin Nutr.* (2014 Apr)
59. Elango R, Humayun MA, Ball RO, Pencharz PB [Evidence that protein requirements have been significantly underestimated.](#) *Curr Opin Clin Nutr Metab Care.* (2010 Jan)
60. Schoenfeld BJ, Aragon AA [How much protein can the body use in a single meal for muscle-building? Implications for daily protein distribution.](#) *J Int Soc Sports Nutr.* (2018 Feb 27)
61. Jäger R, Kerksick CM, Campbell BI, Cribb PJ, Wells SD, Skwiat TM, Purpura M, Ziegenfuss TN, Ferrando AA, Arent SM, Smith-Ryan AE, Stout JR, Arciero PJ, Ormsbee MJ, Taylor LW, Wilborn CD, Kalman DS, Kreider RB, Willoughby DS, Hoffman JR, Krzykowski JL, Antonio J [International Society of Sports Nutrition Position Stand: protein and exercise.](#) *J Int Soc Sports Nutr.* (2017 Jun 20)
62. Thomas DT, Erdman KA, Burke LM [American College of Sports Medicine Joint Position Statement. Nutrition and Athletic Performance.](#) *Med Sci Sports Exerc.* (2016 Mar)
63. Morton RW, McGlory C, Phillips SM [Nutritional interventions to augment resistance training-induced skeletal muscle hypertrophy.](#) *Front Physiol.* (2015 Sep 3)
64. Aragon AA, Schoenfeld BJ [Nutrient timing revisited: is there a post-exercise anabolic window?.](#) *J Int Soc Sports Nutr.* (2013 Jan 29)
65. Clarke R, Refsum H, Birks J, Evans JG, Johnston C, Sherliker P, Ueland PM, Schneede J, McPartlin J, Nexø E, Scott JM [Screening for vitamin B-12 and folate deficiency in older persons.](#) *Am J Clin Nutr.* (2003 May)
66. Rizzo G, Laganà AS, Rapisarda AM, La Ferrera GM, Buscema M, Rossetti P, Nigro A, Muscia V, Valenti G, Sapia F, Sarpietro G, Zigarelli M, Vitale SG [Vitamin B12 among Vegetarians: Status, Assessment and Supplementation.](#) *Nutrients.* (2016 Nov 29)
67. Pawlak R, Lester SE, Babatunde T [The prevalence of cobalamin deficiency among vegetarians assessed by serum vitamin B12: a review of literature.](#) *Eur J Clin Nutr.* (2014 May)
68. Stover PJ [Vitamin B12 and older adults.](#) *Curr Opin Clin Nutr Metab Care.* (2010 Jan)
69. Juzeniene A, Nizauskaite Z [Photodegradation of cobalamins in aqueous solutions and in human blood.](#) *J Photochem Photobiol B.* (2013 May 5)
70. Chapman LE, Darling AL, Brown JE [Association between metformin and vitamin B12 deficiency in patients with type 2 diabetes: A systematic review and meta-analysis.](#) *Diabetes Metab.* (2016 Nov)
71. de Jager J, Kooy A, Lehert P, Wulfelé MG, van der Kolk J, Bets D, Verburg J, Donker AJ, Stehouwer CD [Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial.](#) *BMJ.* (2010 May 20)
72. Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, McQueen MJ, Probstfield J, Fodor G, Held C, Genest J Jr, Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators [Homocysteine lowering with folic acid and B vitamins in vascular disease.](#) *N Engl J Med.* (2006 Apr 13)
73. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline [Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B 6, Folate, Vitamin B 12, Pantothenic Acid, Biotin, and Choline.](#)
74. Xiang F, Lucas R, de Grujil F, Norval M [A systematic review of the influence of skin pigmentation on changes in the concentrations of vitamin D and 25-hydroxyvitamin D in plasma/serum following experimental UV irradiation.](#) *Photochem Photobiol Sci.* (2015 Dec)
75. Meehan M, Penckofer S [The Role of Vitamin D in the Aging Adult.](#) *J Aging Gerontol.* (2014 Dec)
76. Wacker M, Holick MF [Sunlight and Vitamin D: A global perspective for health.](#) *Dermatoendocrinol.* (2013 Jan 1)
77. Ko JA, Lee BH, Lee JS, Park HJ [Effect of UV-B exposure on the concentration of vitamin D2 in sliced shiitake mushroom \(*Lentinus edodes*\) and white button mushroom \(*Agaricus bisporus*\).](#) *J Agric Food Chem.* (2008 May 28)
78. Jasinghe VJ, Perera CO, Barlow PJ [Bioavailability of vitamin D2 from irradiated mushrooms: an in vivo study.](#) *Br J Nutr.* (2005

Jun)

79. Lehmann B, Genehr T, Knuschke P, Pietzsch J, Meurer M [UVB-induced conversion of 7-dehydrocholesterol to 1alpha,25-dihydroxyvitamin D3 in an in vitro human skin equivalent model](#). *J Invest Dermatol*. (2001 Nov)
80. Holick MF, MacLaughlin JA, Clark MB, Holick SA, Potts JT Jr, Anderson RR, Blank IH, Parrish JA, Elias P [Photosynthesis of previtamin D3 in human skin and the physiologic consequences](#). *Science*. (1980 Oct 10)
81. Bikle DD [Vitamin D metabolism and function in the skin](#). *Mol Cell Endocrinol*. (2011 Dec 5)
82. Chakhtoura M, Chamoun N, Rahme M, Fuleihan GE [Impact of vitamin D supplementation on falls and fractures-A critical appraisal of the quality of the evidence and an overview of the available guidelines](#). *Bone*. (2020 Feb)
83. Bischoff-Ferrari HA, Dawson-Hughes B, Orav EJ, Staehelin HB, Meyer OW, Theiler R, Dick W, Willett WC, Egli A [Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline: A Randomized Clinical Trial](#). *JAMA Intern Med*. (2016 Feb)
84. [Lanolin](#). *Drugs and Lactation Database (LactMed®)*. (2006-05)
85. Schlingmann KP, Kaufmann M, Weber S, Irwin A, Goos C, John U, Misselwitz J, Klaus G, Kuwertz-Bröking E, Fehrenbach H, Wingen AM, Güran T, Hoenderop JG, Bindels RJ, Prosser DE, Jones G, Konrad M [Mutations in CYP24A1 and idiopathic infantile hypercalcemia](#). *N Engl J Med*. (2011 Aug 4)
86. Zittermann A, Ernst JB, Gummert JF, Börgermann J [Vitamin D supplementation, body weight and human serum 25-hydroxyvitamin D response: a systematic review](#). *Eur J Nutr*. (2014)
87. Farshidfar F, Pinder MA, Myrie SB [Creatine Supplementation and Skeletal Muscle Metabolism for Building Muscle Mass- Review of the Potential Mechanisms of Action](#). *Curr Protein Pept Sci*. (2017)
88. Chami J, Candow DG [Effect of Creatine Supplementation Dosing Strategies on Aging Muscle Performance](#). *J Nutr Health Aging*. (2019)
89. Candow DG, Forbes SC, Chilibeck PD, Cornish SM, Antonio J, Kreider RB [Effectiveness of Creatine Supplementation on Aging Muscle and Bone: Focus on Falls Prevention and Inflammation](#). *J Clin Med*. (2019 Apr 11)
90. Gualano B, Rawson ES, Candow DG, Chilibeck PD [Creatine supplementation in the aging population: effects on skeletal muscle, bone and brain](#). *Amino Acids*. (2016 Aug)
91. Avgerinos KI, Spyrou N, Bougioukas KI, Kapogiannis D [Effects of creatine supplementation on cognitive function of healthy individuals: A systematic review of randomized controlled trials](#). *Exp Gerontol*. (2018 Jul 15)
92. Stevens JA, Corso PS, Finkelstein EA, Miller TR [The costs of fatal and non-fatal falls among older adults](#). *Inj Prev*. (2006 Oct)
93. Kreider RB, Kalman DS, Antonio J, Ziegenfuss TN, Wildman R, Collins R, Candow DG, Kleiner SM, Almada AL, Lopez HL [International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine](#). *J Int Soc Sports Nutr*. (2017 Jun 13)
94. van der Merwe J, Brooks NE, Myburgh KH [Three weeks of creatine monohydrate supplementation affects dihydrotestosterone to testosterone ratio in college-aged rugby players](#). *Clin J Sport Med*. (2009 Sep)
95. Cook CJ, Crewther BT, Kilduff LP, Drawer S, Gaviglio CM [Skill execution and sleep deprivation: effects of acute caffeine or creatine supplementation - a randomized placebo-controlled trial](#). *J Int Soc Sports Nutr*. (2011 Feb 16)
96. Cooke MB, Brabham B, Buford TW, Shelmadine BD, McPheeters M, Hudson GM, Stathis C, Greenwood M, Kreider R, Willoughby DS [Creatine supplementation post-exercise does not enhance training-induced adaptations in middle to older aged males](#). *Eur J Appl Physiol*. (2014 Jun)
97. Crowe MJ, O'Connor DM, Lukins JE [The effects of beta-hydroxy-beta-methylbutyrate \(HMB\) and HMB/creatine supplementation on indices of health in highly trained athletes](#). *Int J Sport Nutr Exerc Metab*. (2003 Jun)
98. Hoffman J, Ratamess N, Kang J, Mangine G, Faigenbaum A, Stout J [Effect of creatine and beta-alanine supplementation on performance and endocrine responses in strength/power athletes](#). *Int J Sport Nutr Exerc Metab*. (2006 Aug)
99. Eijnde BO, Hespel P [Short-term creatine supplementation does not alter the hormonal response to resistance training](#). *Med Sci Sports Exerc*. (2001 Mar)
100. Volek JS, Ratamess NA, Rubin MR, Gómez AL, French DN, McGuigan MM, Scheett TP, Sharman MJ, Häkkinen K, Kraemer WJ [The effects of creatine supplementation on muscular performance and body composition responses to short-term resistance training overreaching](#). *Eur J Appl Physiol*. (2004 May)
101. Tyka AK, Chwastowski M, Cison T, Palka T, Tyka A, Szygula Z, Pilch W, Strzala M, Cepero M [Effect of creatine malate supplementation on physical performance, body composition and selected hormone levels in sprinters and long-distance runners](#). *Acta Physiol Hung*. (2015 Mar)
102. Sheikholeslami D et al [The effects of creatine supplementation on performance and hormonal response in amateur swimmers](#). *Science & Sport*. (2011 Nov)
103. Arazi H et al. [Effects of short term creatine supplementation and resistance exercises on resting hormonal and cardiovascular responses](#). *Science & Sport*. (2015 Apr)
104. Faraji H et al. [The effects of creatine supplementation on sprint running performance and selected hormonal responses](#). *S Afr J Res Sport Ph*. (2010)
105. Rahimi R et al. [Creatine supplementation alters the hormonal response to resistance exercise](#). *Kinesiology*. (2011)
106. Williamson L, New D [How the use of creatine supplements can elevate serum creatinine in the absence of underlying kidney](#)

[pathology](#). *BMJ Case Rep.* (2014 Sep 19)

107. McCall W, Persky AM [Pharmacokinetics of creatine](#). *Subcell Biochem.* (2007)
108. Poortmans JR, Francaux M [Adverse effects of creatine supplementation: fact or fiction?](#). *Sports Med.* (2000 Sep)
109. Farquhar WB, Zambraski EJ [Effects of creatine use on the athlete's kidney](#). *Curr Sports Med Rep.* (2002 Apr)
110. Pline KA, Smith CL [The effect of creatine intake on renal function](#). *Ann Pharmacother.* (2005 Jun)
111. Francaux M, Poortmans JR [Side effects of creatine supplementation in athletes](#). *Int J Sports Physiol Perform.* (2006 Dec)
112. Persky AM, Rawson ES [Safety of creatine supplementation](#). *Subcell Biochem.* (2007)
113. Kim HJ, Kim CK, Carpentier A, Poortmans JR [Studies on the safety of creatine supplementation](#). *Amino Acids.* (2011 May)
114. Gualano B, Roschel H, Lancha AH Jr, Brightbill CE, Rawson ES [In sickness and in health: the widespread application of creatine supplementation](#). *Amino Acids.* (2012 Aug)
115. Gualano B, Ferreira DC, Sapienza MT, Seguro AC, Lancha AH Jr [Effect of short-term high-dose creatine supplementation on measured GFR in a young man with a single kidney](#). *Am J Kidney Dis.* (2010 Mar)
116. Gualano B, de Salles Painelli V, Roschel H, Lugaesi R, Dorea E, Artioli GG, Lima FR, da Silva ME, Cunha MR, Seguro AC, Shimizu MH, Otaduy MC, Sapienza MT, da Costa Leite C, Bonfá E, Lancha Junior AH [Creatine supplementation does not impair kidney function in type 2 diabetic patients: a randomized, double-blind, placebo-controlled, clinical trial](#). *Eur J Appl Physiol.* (2011 May)
117. Taes YE, Delanghe JR, De Bacquer D, Langlois M, Stevens L, Geerolf I, Lameire NH, De Vriese AS [Creatine supplementation does not decrease total plasma homocysteine in chronic hemodialysis patients](#). *Kidney Int.* (2004 Dec)
118. Shelmadine D et al. [The effects of supplementation of creatine on total homocysteine](#). *JRN.* (2013 Sep)
119. Syrotuik DG, Bell GJ [Acute creatine monohydrate supplementation: a descriptive physiological profile of responders vs. nonresponders](#). *J Strength Cond Res.* (2004 Aug)
120. Hadjicharalambous M, Kilduff LP, Pitsiladis YP [Brain serotonin and dopamine modulators, perceptual responses and endurance performance during exercise in the heat following creatine supplementation](#). *J Int Soc Sports Nutr.* (2008 Sep 30)
121. Sato K, Iemitsu M [The Role of Dehydroepiandrosterone \(DHEA\) in Skeletal Muscle](#). *Vitam Horm.* (2018)
122. Gonzales-Arimborgo C, Yupanqui I, Montero E, Alarcón-Yaquetto DE, Zevallos-Concha A, Caballero L, Gasco M, Zhao J, Khan IA, Gonzales GF [Acceptability, Safety, and Efficacy of Oral Administration of Extracts of Black or Red Maca \(*Lepidium meyenii*\) in Adult Human Subjects: A Randomized, Double-Blind, Placebo-Controlled Study](#). *Pharmaceuticals (Basel).* (2016 Aug 18)
123. Gonzales GF, Córdova A, Vega K, Chung A, Villena A, Góñez C, Castillo S [Effect of *Lepidium meyenii* \(MACA\) on sexual desire and its absent relationship with serum testosterone levels in adult healthy men](#). *Andrologia.* (2002 Dec)
124. Brooks NA, Wilcox G, Walker KZ, Ashton JF, Cox MB, Stojanovska L [Beneficial effects of *Lepidium meyenii* \(Maca\) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content](#). *Menopause.* (2008 Nov-Dec)
125. Dording CM, Fisher L, Papakostas G, Farabaugh A, Sonawalla S, Fava M, Mischoulon D [A double-blind, randomized, pilot dose-finding study of maca root \(*L. meyenii*\) for the management of SSRI-induced sexual dysfunction](#). *CNS Neurosci Ther.* (2008 Fall)
126. Dording CM, Schettler PJ, Dalton ED, Parkin SR, Walker RS, Fehling KB, Fava M, Mischoulon D [A double-blind placebo-controlled trial of maca root as treatment for antidepressant-induced sexual dysfunction in women](#). *Evid Based Complement Alternat Med.* (2015)
127. Zenico T, Cicero AF, Valmorri L, Mercuriali M, Bercovich E [Subjective effects of *Lepidium meyenii* \(Maca\) extract on well-being and sexual performances in patients with mild erectile dysfunction: a randomised, double-blind clinical trial](#). *Andrologia.* (2009 Apr)
128. Erem S, Atfi A, Razzaque MS [Anabolic effects of vitamin D and magnesium in aging bone](#). *J Steroid Biochem Mol Biol.* (2019 Oct)
129. Severino P, Netti L, Mariani MV, Maraone A, D'Amato A, Scarpato R, Infusino F, Pucci M, Lavalle C, Maestrini V, Mancone M, Fedele F [Prevention of Cardiovascular Disease: Screening for Magnesium Deficiency](#). *Cardiol Res Pract.* (2019 May 2)
130. Shahi A, Aslani S, Ataollahi M, Mahmoudi M [The role of magnesium in different inflammatory diseases](#). *Inflammopharmacology.* (2019 Aug)
131. Xue W, You J, Su Y, Wang Q [The Effect of Magnesium Deficiency on Neurological Disorders: A Narrative Review Article](#). *Iran J Public Health.* (2019 Mar)
132. Kirkland AE, Sarlo GL, Holton KF [The Role of Magnesium in Neurological Disorders](#). *Nutrients.* (2018 Jun 6)
133. Veronese N, Zurlò A, Solmi M, Luchini C, Trevisan C, Bano G, Manzano E, Sergi G, Rylander R [Magnesium Status in Alzheimer's Disease: A Systematic Review](#). *Am J Alzheimers Dis Other Dement.* (2016 May)
134. Held K, Antonijevic IA, Künzel H, Uhr M, Wetter TC, Golly IC, Steiger A, Murck H [Oral Mg\(2+\) supplementation reverses age-related neuroendocrine and sleep EEG changes in humans](#). *Pharmacopsychiatry.* (2002 Jul)
135. Nielsen FH, Johnson LK, Zeng H [Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep](#). *Magnes Res.* (2010 Dec)
136. Maggio M, De Vita F, Lauretani F, Nouvenne A, Meschi T, Ticinesi A, Dominguez LJ, Barbagallo M, Dall'aglio E, Ceda GP [The](#)

- [Interplay between Magnesium and Testosterone in Modulating Physical Function in Men. *Int J Endocrinol.* \(2014\)](#)
137. Ford ES, Mokdad AH [Dietary magnesium intake in a national sample of US adults. *J Nutr.* \(2003 Sep\)](#)
 138. Musso CG [Magnesium metabolism in health and disease. *Int Urol Nephrol.* \(2009\)](#)
 139. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT [Hypomagnesemia in patients with type 2 diabetes. *Clin J Am Soc Nephrol.* \(2007 Mar\)](#)
 140. Sarafidis PA, Georgianos PI, Lasaridis AN [Diuretics in clinical practice. Part II: electrolyte and acid-base disorders complicating diuretic therapy. *Expert Opin Drug Saf.* \(2010 Mar\)](#)
 141. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes [Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.](#)
 142. Pazianas M, Abrahamsen B, Ferrari S, Russell RG [Eliminating the need for fasting with oral administration of bisphosphonates. *Ther Clin Risk Manag.* \(2013\)](#)
 143. Witkowski M, Hubert J, Mazur A [Methods of assessment of magnesium status in humans: a systematic review. *Magnes Res.* \(2011 Dec\)](#)
 144. Yoshimura Y, Fujisaki K, Yamamoto T, Shinohara Y [Pharmacokinetic Studies of Orally Administered Magnesium Oxide in Rats. *Yakugaku Zasshi.* \(2017 May 1\)](#)
 145. Firoz M, Graber M [Bioavailability of US commercial magnesium preparations. *Magnes Res.* \(2001 Dec\)](#)
 146. Walker AF, Marakis G, Christie S, Byng M [Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. *Magnes Res.* \(2003 Sep\)](#)
 147. Lindberg JS, Zobitz MM, Poindexter JR, Pak CY [Magnesium bioavailability from magnesium citrate and magnesium oxide. *J Am Coll Nutr.* \(1990 Feb\)](#)
 148. Fu X, Shen X, Finnan EG, Haytowitz DB, Booth SL [Measurement of Multiple Vitamin K Forms in Processed and Fresh-Cut Pork Products in the U.S. Food Supply. *J Agric Food Chem.* \(2016 Jun 8\)](#)
 149. Manoury E, Jourdon K, Boyaval P, Fourcassié P [Quantitative measurement of vitamin K2 \(menaquinones\) in various fermented dairy products using a reliable high-performance liquid chromatography method. *J Dairy Sci.* \(2013 Mar\)](#)
 150. Booth SL [Vitamin K: food composition and dietary intakes. *Food Nutr Res.* \(2012\)](#)
 151. Kamao M, Suhara Y, Tsugawa N, Uwano M, Yamaguchi N, Uenishi K, Ishida H, Sasaki S, Okano T [Vitamin K content of foods and dietary vitamin K intake in Japanese young women. *J Nutr Sci Vitaminol \(Tokyo\).* \(2007 Dec\)](#)
 152. Elder SJ, Haytowitz DB, Howe J, Peterson JW, Booth SL [Vitamin k contents of meat, dairy, and fast food in the u.s. Diet. *J Agric Food Chem.* \(2006 Jan 25\)](#)
 153. Schurgers LJ, Vermeer C [Determination of phyloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations. *Haemostasis.* \(2000 Nov-Dec\)](#)
 154. Booth SL, Pennington JA, Sadowski JA [Food sources and dietary intakes of vitamin K-1 \(phyloquinone\) in the American diet: data from the FDA Total Diet Study. *J Am Diet Assoc.* \(1996 Feb\)](#)
 155. Shimogawara K, Muto S [Purification of Chlamydomonas 28-kDa ubiquitinated protein and its identification as ubiquitinated histone H2B. *Arch Biochem Biophys.* \(1992 Apr\)](#)
 156. Hirauchi K, Sakano T, Notsumoto S, Nagaoka T, Morimoto A, Fujimoto K, Masuda S, Suzuki Y [Measurement of K vitamins in animal tissues by high-performance liquid chromatography with fluorimetric detection. *J Chromatogr.* \(1989 Dec 29\)](#)
 157. Institute of Medicine (US) Panel on Micronutrients [Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.](#)
 158. De Jesus Moreno Moreno M [Cognitive improvement in mild to moderate Alzheimer's dementia after treatment with the acetylcholine precursor choline alfoscerate: a multicenter, double-blind, randomized, placebo-controlled trial. *Clin Ther.* \(2003 Jan\)](#)
 159. Lippelt DP, van der Kint S, van Herk K, Naber M [No Acute Effects of Choline Bitartrate Food Supplements on Memory in Healthy, Young, Human Adults. *PLoS One.* \(2016 Jun 24\)](#)
 160. Parisi V, Coppola G, Centofanti M, Oddone F, Angrisani AM, Ziccardi L, Ricci B, Quaranta L, Manni G [Evidence of the neuroprotective role of citicoline in glaucoma patients. *Prog Brain Res.* \(2008\)](#)
 161. Meissner HO, Mscisz A, Reich-Bilinska H, Kapczynski W, Mrozikiewicz P, Bobkiewicz-Kozłowska T, Kedzia B, Lowicka A, Barchia I [Hormone-Balancing Effect of Pre-Gelatinized Organic Maca \(*Lepidium peruvianum* Chacon\): \(II\) Physiological and Symptomatic Responses of Early-Postmenopausal Women to Standardized doses of Maca in Double Blind, Randomized, Placebo-Controlled, Multi-Centre Clinical Study. *Int J Biomed Sci.* \(2006 Dec\)](#)
 162. Meissner HO, Kapczynski W, Mscisz A, Lutomski J [Use of gelatinized maca \(*lepidium peruvianum*\) in early postmenopausal women. *Int J Biomed Sci.* \(2005 Jun\)](#)
 163. Meissner HO, Mscisz A, Reich-Bilinska H, Mrozikiewicz P, Bobkiewicz-Kozłowska T, Kedzia B, Lowicka A, Barchia I [Hormone-Balancing Effect of Pre-Gelatinized Organic Maca \(*Lepidium peruvianum* Chacon\): \(III\) Clinical responses of early-postmenopausal women to Maca in double blind, randomized, Placebo-controlled, crossover configuration, outpatient study. *Int J Biomed Sci.* \(2006 Dec\)](#)
 164. Stojanovska L, Law C, Lai B, Chung T, Nelson K, Day S, Apostolopoulos V, Haines C [Maca reduces blood pressure and](#)

- depression, in a pilot study in postmenopausal women. *Climacteric*. (2015 Feb)
165. Takewaka1 T and Hara K [Clinical Effect of Oral Administration of Maca \(*Lepidium meyenii*\) Extract on Japanese Peri-Menopausal Women Subjects: A Randomized, Double-Blind, Placebo-Controlled Study](#). *IJBSE*. (2019 Mar)
 166. Pae M, Wu D [Nutritional modulation of age-related changes in the immune system and risk of infection](#). *Nutr Res*. (2017 May)
 167. Koekkoek WA, van Zanten AR [Antioxidant Vitamins and Trace Elements in Critical Illness](#). *Nutr Clin Pract*. (2016 Aug)
 168. Traber MG [Vitamin E and K interactions--a 50-year-old problem](#). *Nutr Rev*. (2008 Nov)
 169. Emami MR, Safabakhsh M, Alizadeh S, Asbaghi O, Khosroshahi MZ [Effect of vitamin E supplementation on blood pressure: a systematic review and meta-analysis](#). *J Hum Hypertens*. (2019 Jul)
 170. Institute of Medicine (US) Panel on Dietary Antioxidants and Related Compounds [Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids](#).
 171. Lim J, Henry CJ, Haldar S [Vinegar as a functional ingredient to improve postprandial glycemic control-human intervention findings and molecular mechanisms](#). *Mol Nutr Food Res*. (2016 Aug)
 172. Shishehbor F, Mansoori A, Shirani F [Vinegar consumption can attenuate postprandial glucose and insulin responses: a systematic review and meta-analysis of clinical trials](#). *Diabetes Res Clin Pract*. (2017 May)
 173. Kondo T, Kishi M, Fushimi T, Ugajin S, Kaga T [Vinegar intake reduces body weight, body fat mass, and serum triglyceride levels in obese Japanese subjects](#). *Biosci Biotechnol Biochem*. (2009 Aug)
 174. Derakhshandeh-Rishehri SM, Heidari-Beni M, Feizi A, Askari GR, Entezari MH [Effect of honey vinegar syrup on blood sugar and lipid profile in healthy subjects](#). *Int J Prev Med*. (2014 Dec)
 175. Johnston CS, White AM, Kent SM [Preliminary evidence that regular vinegar ingestion favorably influences hemoglobin A1c values in individuals with type 2 diabetes mellitus](#). *Diabetes Res Clin Pract*. (2009 May)
 176. Gheflati A, Bashiri R, Ghadiri-Anari A, Reza JZ, Kord MT, Nadjarzadeh A [The effect of apple vinegar consumption on glycemic indices, blood pressure, oxidative stress, and homocysteine in patients with type 2 diabetes and dyslipidemia: A randomized controlled clinical trial](#). *Clin Nutr ESPEN*. (2019 Oct)
 177. Jasbi P, Baker O, Shi X, Gonzalez LA, Wang S, Anderson S, Xi B, Gu H, Johnston CS [Daily red wine vinegar ingestion for eight weeks improves glucose homeostasis and affects the metabolome but does not reduce adiposity in adults](#). *Food Funct*. (2019 Nov 1)
 178. Panetta C, Jonk Y, Shapiro A [Prospective randomized clinical trial evaluating the impact of vinegar on lipids in non-diabetics](#). *WJCD*. (2013 Apr)
 179. Soleymani T, Lo Sicco K, Shapiro J [The Infatuation With Biotin Supplementation: Is There Truth Behind Its Rising Popularity? A Comparative Analysis of Clinical Efficacy versus Social Popularity](#). *J Drugs Dermatol*. (2017 May 1)
 180. John JJ, Cooley V, Lipner SR [Assessment of biotin supplementation among patients in an outpatient dermatology clinic](#). *J Am Acad Dermatol*. (2019 Aug)
 181. Patel DP, Swink SM, Castelo-Soccio L [A Review of the Use of Biotin for Hair Loss](#). *Skin Appendage Disord*. (2017 Aug)
 182. Trüeb RM [Serum Biotin Levels in Women Complaining of Hair Loss](#). *Int J Trichology*. (2016 Apr-Jun)
 183. Zempleni J, Hassan YI, Wijeratne SS [Biotin and biotinidase deficiency](#). *Expert Rev Endocrinol Metab*. (2008 Nov 1)
 184. Lipner SR, Scher RK [Biotin for the treatment of nail disease: what is the evidence?.](#) *J Dermatolog Treat*. (2018 Jun)
 185. Colombo VE, Gerber F, Bronhofer M, Floersheim GL [Treatment of brittle fingernails and onychoschizia with biotin: scanning electron microscopy](#). *J Am Acad Dermatol*. (1990 Dec)
 186. Hochman LG, Scher RK, Meyerson MS [Brittle nails: response to daily biotin supplementation](#). *Cutis*. (1993 Apr)
 187. Gloster H Jr, Kindred C [Habit-tic-like and median nail-like dystrophies treated with multivitamins](#). *J Am Acad Dermatol*. (2005 Sep)
 188. Möhrenschrager M et al. [Recalcitrant trachyonychia of childhood – response to daily oral biotin supplementation: report of two cases](#). *J. Dermatol. Treat.*. (2009 Jul)
 189. Piraccini B et al. [Triangular worn-down nails: Report of 14 cases](#). *Giornale Italiano di Dermatologia e Venereologia*. (2005 Jan)
 190. Boccaletti V, Zendri E, Giordano G, Gnetti L, De Panfilis G [Familial Uncombable Hair Syndrome: Ultrastructural Hair Study and Response to Biotin](#). *Pediatr Dermatol*. (2007 May-Jun)
 191. Shelley WB, Shelley ED [Uncombable hair syndrome: observations on response to biotin and occurrence in siblings with ectodermal dysplasia](#). *J Am Acad Dermatol*. (1985 Jul)
 192. Mercke Y, Sheng H, Khan T, Lippmann S [Hair loss in psychopharmacology](#). *Ann Clin Psychiatry*. (2000 Mar)
 193. Schulpis KH, Karikas GA, Tjamouranis J, Regoutas S, Tsakiris S [Low serum biotinidase activity in children with valproic acid monotherapy](#). *Epilepsia*. (2001 Oct)
 194. Wang X, Wang H, Xu D, Zhu L, Liu L [Risk of valproic acid-related alopecia: A systematic review and meta-analysis](#). *Seizure*. (2019 Jul)
 195. Geller AI, Shehab N, Weidle NJ, Lovegrove MC, Wolpert BJ, Timbo BB, Mozersky RP, Budnitz DS [Emergency Department Visits for Adverse Events Related to Dietary Supplements](#). *N Engl J Med*. (2015 Oct 15)

196. Busti F, Campostrini N, Martinelli N, Girelli D [Iron deficiency in the elderly population, revisited in the hepcidin era.](#) *Front Pharmacol.* (2014 Apr 23)
197. Smith DL [Anemia in the elderly.](#) *Am Fam Physician.* (2000 Oct 1)
198. Basu A, Rhone M, Lyons TJ [Berries: emerging impact on cardiovascular health.](#) *Nutr Rev.* (2010 Mar)
199. Anderson RL, Wolf WJ [Compositional changes in trypsin inhibitors, phytic acid, saponins and isoflavones related to soybean processing.](#) *J Nutr.* (1995 Mar)
200. Erdman JW Jr, Badger TM, Lampe JW, Setchell KD, Messina M [Not all soy products are created equal: caution needed in interpretation of research results.](#) *J Nutr.* (2004 May)
201. Barzel US, Massey LK [Excess dietary protein can adversely affect bone.](#) *J Nutr.* (1998 Jun)
202. Schwingshackl L, Hoffmann G [Comparison of high vs. normal/low protein diets on renal function in subjects without chronic kidney disease: a systematic review and meta-analysis.](#) *PLoS One.* (2014 May 22)
203. Hunt JR, Johnson LK, Fariba Roughead ZK [Dietary protein and calcium interact to influence calcium retention: a controlled feeding study.](#) *Am J Clin Nutr.* (2009 May)
204. Wright CS, Li J, Campbell WW [Effects of Dietary Protein Quantity on Bone Quantity following Weight Loss: A Systematic Review and Meta-analysis.](#) *Adv Nutr.* (2019 Nov 1)
205. Livingstone C [Insulin-like growth factor-I \(IGF-I\) and clinical nutrition.](#) *Clin Sci (Lond).* (2013 Sep)
206. Yakar S, Rosen CJ, Beamer WG, Ackert-Bicknell CL, Wu Y, Liu JL, Ooi GT, Setser J, Frystyk J, Boisclair YR, LeRoith D [Circulating levels of IGF-1 directly regulate bone growth and density.](#) *J Clin Invest.* (2002 Sep)